⇒> file reg

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STRUCTURE FILE UPDATES: 20 JAN 2003 HIGHEST RN 479577-81-6 DICTIONARY FILE UPDATES: 20 JAN 2003 HIGHEST RN 479577-81-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> file hcaplus FILE 'HCAPLUS' ENTERED AT 14:21:17 ON 21 JAN 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 21 Jan 2003 VOL 138 ISS 4 FILE LAST UPDATED: 20 Jan 2003 (20030120/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 124 L3STR

`CH2 08 Ò 7

2, 167 structures from this query

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

REP G1 = (0-3) CNODE ATTRIBUTES: CONNECT IS E1 RC AT DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS

STEREO ATTRIBUTES: NONE

L5

2167 SEA FILE=REGISTRY SSS FUL L3

L16

CH2-C-V-0

STR

016 17 18

5 wheet search 2139 shudwes

9 G2, 1 G1 `CH2 08

CH2-OH **@10 11** 

> CH2-O--- C--- O @12 13 14 15

REP G1 = (0-3) C VAR G2=H/AK/10/12/16 NODE ATTRIBUTES: CONNECT IS E1 RC AT CONNECT IS E1 RC AT 1 CONNECT IS E1 RC AT 1 DEFAULT MLEVEL IS ATOM 15 DEFAULT ECLEVEL IS LIMITED

**GRAPH ATTRIBUTES:** 

RSPEC I

NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

2139 SEA FILE=REGISTRY SUB=L5 SSS FUL L16 L18

L19

L20

1246 SEA FILE=HCAPLUS ABB=ON L18
30 SEA FILE=HCAPLUS ABB=ON L19(L)THU/RL
715 SEA FILE=HCAPLUS ABB=ON L19(L)(PREP OR SPN OR IMF)/RL
21 SEA FILE=HCAPLUS ABB=ON L20 AND L21 L21

L24

=> d 124 all 1-21 hitstr

prip for therapeuticuse

L24 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2003 ACS 2002:955399 HCAPLUS AN

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

```
Sackey 09/937386 Page 3
     138:33370
DN
     Hyaluronic acid production enhancer as skin protectant
TI
     Tanaka, Shinji; Murobuse, Kimiko; Kobayashi, Akiyuki
IN
     NOF Corporation, Japan
PA
     Jpn. Kokai Tokkyo Koho, 20 pp.
SO
     CODEN: JKXXAF
DT
     Patent
LA
     Japanese
     ICM A61K031-661
IC
     ICS A61K038-00; A61P017-02; A61P043-00; C07F009-6574
     1-12 (Pharmacology)
CC
     Section cross-reference(s): 24
FAN. CNT 1
                      KIND DATE
                                            APPLICATION NO.
                                                             DATE
     PATENT NO.
                            20021218
                                            JP 2001-171689
                                                             20010606
     JP 2002363081
                       A2
                            20010606
PRAI JP 2001-171689
GI
CH<sub>2</sub>OR
     þ. 0
CHO
CH20 ~
        0
     Skin protectants in the treatment of atrophy of the skin induced by aging
AB
     or steroid and in the prevention of the scar formation after the healing
     of wound which contain as the active ingredient cyclic phosphatide derivs.
     represented by the following general formula I (RO = C8-22 alc. residue or
     fatty acid residue; M = H, alkali metal, alk. earths metal, and
     (substituted) ammonium) as hyaluronic acid prodn. enhancer, hyaluronic
     acid synthetase gene promoter, and cellular activator are offered.
     cyclic phosphatide deriv hyaluronate enhancer skin protectant
ST
IT
     Skin, disease
        {aging; cyclic phosphatide as hyaluronic acid prodn. enhancer for
        protecting skin)
ΙT
     Skin, disease
        (atrophy; cyclic phosphatide as hyaluronic acid prodn. enhancer for
        protecting skin)
     Cell activation
TΤ
     Wound healing promoters
         (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting
     Phosphatidic acids
IT
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
         (cyclic, derivs.; cyclic phosphatide as hyaluronic acid prodn. enhancer
        for protecting skin)
ΙT
     Gene, animal
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (hyaluronic acid synthetase; cyclic phosphatide as hyaluronic acid
        prodn. enhancer for protecting skin)
IT
     Skin, disease
         (scar; cyclic phosphatide as hyaluronic acid prodn. enhancer for
```

(synergistic; cyclic phosphatide as hyaluronic acid prodn. enhancer for

protecting skin)
Drug interactions

IT

protecting skin) 9004-61-9, Hyaluronic acid 39346-43-5, Hyaluronic acid synthetase IT RL: BSU (Biological study, unclassified); BIOL (Biological study) (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting skin) 106096-93-9P, Basic fibroblast growth factor 168217-08-1P IT 168217-09-2P 169736-88-3P 478336-74-2P 478336-75-3P 478336-76-4P 478336-77-5P 478336-78-6P 478336-79-7P 478336-80-0P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting skin) 506-03-6, 1-0-sn-Hexadecylglycerol IT RL: RCT (Reactant); RACT (Reactant or reagent) (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting skin) 168217-08-1P 168217-09-2P 169736-88-3P IΤ 478336-74-2P 478336-75-3P 478336-76-4P 478336-77-5P 478336-78-6P 478336-79-7P 478336-80-0P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting skin) RN 168217-08-1 HCAPLUS Hexadecanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-CN yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na 🗬

168217-09-2 HCAPLUS RNCN

9-Hexadecenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4yl}methyl ester, sodium salt, (92)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

Na

RN 169736-88-3 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HO P R 
$$(CH_2)$$
  $7$   $Z$   $(CH_2)$   $7$   $Z$ 

Na

RN 478336-74-2 HCAPLUS

CN 5,8,11,14,17-Eicosapentaenoic acid, {(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

HO P R (CH<sub>2</sub>) 
$$\frac{\overline{z}}{\overline{z}}$$
  $\overline{\overline{z}}$   $\overline{\overline{z}}$ 

Na

PAGE 1-B

RN 478336-75-3 HCAPLUS

CN 4,7,10,13,16,19-Docosahexaenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (4Z,7Z,10Z,13Z,16Z,19Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

Na

PAGE 1-B

RN 478336-76-4 HCAPLUS

Absolute stereochemistry.

Na

RN 478336-77-5 HCAPLUS

CN 1,3,2-Dioxaphospholane, 4-[[(9Z)-9-hexadecenyloxy]methyl]-2-hydroxy-, 2-oxide, sodium salt, (4R)- (9CI) (CA INDEX NAME)

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

Absolute stereochemistry.

Double bond geometry as shown.

Na

RN 478336-78-6 HCAPLUS

CN 1,3,2-Dioxaphospholane, 2-hydroxy-4-[[(9Z)-9-octadecenyloxy]methyl]-,
2-oxide, sodium salt, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

Na

RN 478336-79-7 HCAPLUS

CN 1,3,2-Dioxaphospholane, 4-[[(52,82,112,142,172)-5,8,11,14,17-eicosapentaenyloxy]methyl]-2-hydroxy-, 2-oxide, sodium salt, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

Na

PAGE 1-B

Z

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

RN 478336-80-0 HCAPLUS
CN 1,3,2-Dioxaphospholane, 4-[(42,72,102,132,162,192)-4,7,10,13,16,19docosahexaenyloxy]methyl]-2-hydroxy-, 2-oxide, sodium salt, (4R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

Na

PAGE 1-B



L24 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:693051 HCAPLUS

DN 135:242705

TI Phosphate based biodegradable polymers, their preparation and compositions with a biologically active substance

IN Leong, Kam; Jie, Wen; Zhuo, Ren-Xi; Mao, Hai-Quan

PA Johns Hopkins University, USA

SO PCT Int. Appl., 126 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K009-00

ICS A61K009-14; A61K009-16; A61M005-00; C08G079-04

CC 35-7 (Chemistry of Synthetic High Polymers)

Section cross-reference(s): 63

FAN. CNT 1

APPLICATION NO. DATE PATENT NO. KIND DATE ----20010920 WO 2001-US7603 20010310 WO 2001068052 A2 PΙ W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 2001-803358 20010310 US 2002155092

```
20000310
PRAI US 2000-188477P
                      P
    Biodegradable polymers comprise repeat units derived from cyclic phosphate
    monomers and, optionally, repeat units derived from lactide or
     caprolactone monomers. Articles and microspheres are prepd. from
     biodegradable polymers and polymer compns. Controlled release of a biol.
     active substance is achieved using the biodegradable polymers.
     D, L-lactide and ethylene Me phosphate (prepn. given) were polymd. in the
    presence of aluminum triisopropoxide under Ar at 140-160.degree..
     lactide ethylene methyl phosphate copolymer manuf property; ethylene
ST
    methyl phosphate prepn polymn; block polymn lactide ethylene methyl
     phosphate; ring opening polymn lactide ethylene methyl phosphate
     Polymers, preparation
IT
     RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (biodegradable, biocompatible; phosphate-based biodegradable polymers
        for controlled-release of biol. active substances)
IT
     Polymerization
        (block; of lactide and ethylene Me phosphate)
IT
     Drug delivery systems
        (controlled-release; phosphate-based biodegradable polymers for)
     Glass transition temperature
IT
     Polymer degradation
        (of phosphate-based biodegradable polymers for controlled-release of
        biol. active substances)
     Polyesters, preparation
TT
     RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
IT
     Polymerization
        (ring-opening; of lactide and ethylene Me phosphate)
     361186-26-7P
IT
     RL: IMF (Industrial manufacture); PREP (Preparation)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
     220490-57-3P, Lactide-ethylene methyl phosphate copolymer
TT
     361186-24-5P 361186-25-6DP, demethylation
     RL: IMF (Industrial manufacture); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
                 6609-64-9P
TΤ
     822-39-9P
     RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT
     (Reactant or reagent)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
     326604-67-5, Lactide-ethyl ethylene phosphate copolymer
IT
     RL: PRP (Properties)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
     100-01-6, p-Nitroaniline, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
     361186-25-6P
IT
     RL: IMF (Industrial manufacture); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. and block polymn.; phosphate-based biodegradable polymers for
```

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Sackey 09/937386 Page 10
```

controlled-release of biol. active substances) 2196-04-5P, Ethylene methyl phosphate IT RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent) (prepn. and polymn.; phosphate-based biodegradable polymers for controlled-release of biol. active substances) 7719-12-2, Phosphorus trichloride IT RL: RCT (Reactant); RACT (Reactant or reagent) (reaction with ethylene glycol; phosphate-based biodegradable polymers for controlled-release of biol. active substances) 107-21-1, Ethylene glycol, reactions IT RL: RCT (Reactant); RACT (Reactant or reagent) (reaction with phosphorus trichloride; phosphate-based biodegradable polymers for controlled-release of biol. active substances) IT 361186-26-7P RL: IMF (Industrial manufacture); PREP (Preparation) (phosphate-based biodegradable polymers for controlled-release of biol. active substances) RN 361186-26-7 HCAPLUS 2-Oxepanone, polymer with 2-ethoxy-1,3,2-dioxaphospholane 2-oxide, block CN (CA INDEX NAME) CM 1 CRN 823-31-4 CMF C4 H9 O4 P 2 CM CRN 502-44-3 CMF C6 H10 O2 220490-57-3P, Lactide-ethylene methyl phosphate copolymer IT 361186-24-5P 361186-25-6DP, demethylation RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (phosphate-based biodegradable polymers for controlled-release of biol. active substances) 220490-57-3 HCAPLUS RN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 2-methoxy-1,3,2-CN dioxaphospholan 2-oxide (9CI) (CA INDEX NAME)

CRN 2196-04-5 CMF C3 H7 O4 P

CM 2

CRN 95-96-5 CMF C6 H8 O4

CN

361186-24-5 HCAPLUS RN

1,3,2-Dioxaphospholane, 2-methoxy-, 2-oxide, polymer with alpha.-hydro-.omega.-hydroxy[poly(oxy-1,2-ethanediyl)] disodium salt, block (9CI) (CA INDEX NAME)

CM 1

CRN 50856-01-4 CMF (C2 H4 O)n H2 O . 2 Na CCI PMS

●2 Na

CM 2

CRN 2196-04-5 CMF C3 H7 O4 P

RN 361186-25-6 HCAPLUS CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, (3S,6S)-, polymer with

2-methoxy-1, 3, 2-dioxaphospholane 2-oxide, block (9CI) (CA INDEX NAME)

CM 1

CRN 4511-42-6 CMF C6 H8 O4

Absolute stereochemistry.

CM 2

CRN 2196-04-5 CMF C3 H7 O4 P

IT 361186-25-6P

RL: IMF (Industrial manufacture); PRP (Properties); THU

(Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(prepn. and block polymn.; phosphate-based biodegradable polymers for controlled-release of biol. active substances)

RN 361186-25-6 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, (3S,6S)-, polymer with

2-methoxy-1, 3, 2-dioxaphospholane 2-oxide, block (9CI) (CA INDEX NAME)

CM 1

CRN 4511-42-6 CMF C6 H8 O4

Absolute stereochemistry.

CM 2

CRN 2196-04-5 CMF C3 H7 O4 P

IT 2196-04-5P, Ethylene methyl phosphate
RL: IMF (Industrial manufacture); RCT (Reactant); PREP
(Preparation); RACT (Reactant or reagent)
(prepn. and polymn.; phosphate-based biodegradable polymers for controlled-release of biol. active substances)

RN 2196-04-5 HCAPLUS

CN 1,3,2-Dioxaphospholane, 2-methoxy-, 2-oxide (9CI) (CA INDEX NAME)

L24 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2003 ACS AN 2001:380438 HCAPLUS DN 135:24657 TI Selective cellular targeting: multifunctional delivery vehicles IN Glazier, Arnold PA Drug Innovation + Design, Inc., USA SO PCT Int. Appl., 981 pp. CODEN: PIXXD2 ÐΤ Patent LA English ICM A61K047-48 IC 63-5 (Pharmaceuticals) Section cross-reference(s): 1, 2, 8, 15, 25, 28 FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ------\_\_\_\_\_ PΙ WO 2001036003 A2 20010525 WO 2000-US31262 20001114 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

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SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                            20010530
                                              AU 2001-16075
                                                                 20001114
     AU 2001016075
                        A5
                                                                20001114
                                              EP 2000-978631
                              20021113
                        A1
     EP 1255567
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
         R:
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                              19991115
PRAI US 1999-165485P
                        P
     US 2000-239478P
                        P
                              20001011
     US 2000-241937P
                              20001020
                        Ρ
     WO 2000-US31262
                        W
                              20001114
     The present invention relates to the compns., methods, and applications of
AB
     a novel approach to selective cellular targeting. The purpose of this
     invention is to enable the selective delivery and/or selective activation
     of effector mols. to target cells for diagnostic or therapeutic purposes.
     The present invention relates to multi-functional prodrugs or targeting
     vehicles wherein each functionality is capable of enhancing targeting
     selectivity, affinity, intracellular transport, activation or
     detoxification. The present invention also relates to ultralow dose, multiple target, multiple drug chemotherapy and targeted immunotherapy for
     cancer treatment.
     antitumor drug targeting delivery vehicle
ST
     Multidrug resistance proteins
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (MDR1, inhibitors; multifunctional delivery vehicles for selective
         cellular targeting of drugs)
     Glycoproteins, specific or class
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (P170, inhibitors; multifunctional delivery vehicles for selective
         cellular targeting of drugs)
IT
     Prostate gland
         (adenocarcinoma; multifunctional delivery vehicles for selective
         cellular targeting of drugs)
IT
     Receptors
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
      (Process)
         (cell-surface; multifunctional delivery vehicles for selective cellular
         targeting of drugs)
     Cholecystokinin receptors
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
      (Process)
         (cholecystokinin B; multifunctional delivery vehicles for selective
         cellular targeting of drugs)
     Proteins, specific or class
IT
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
      study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
      (Process)
         (complexes; multifunctional delivery vehicles for selective cellular
         targeting of drugs)
      Proteins, specific or class
TT
      RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
      study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
      (Process)
         (fibroblast-activating; multifunctional delivery vehicles for selective
         cellular targeting of drugs)
TT
      Receptors
```

IΤ

TT

IT

IT

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (folate; multifunctional deliv ry vehicles for selective cellular targeting of drugs)
Receptors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological

study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
(Process)
 (for bombesin-releasing peptide; multifunctional delivery vehicles for
 selective cellular targeting of drugs)

Receptors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
(Process)

(for gastrin-releasing peptide; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Transport proteins
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (for nucleosides, inhibitors; multifunctional delivery vehicles for selective cellular targeting of drugs)

Biological transport (intracellular; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Antitumor agents
Cell division
Chelating agents
Cytotoxic agents
Drug targeting
Imaging agents
Immunization

Immunostimulants
 (multifunctional delivery vehicles for selective cellular targeting of
 drugs)

IT Enzymes, biological studies
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 (multifunctional delivery vehicles for selective cellular targeting of

(multifunctional delivery vehicles for selective cellular targeting of drugs)
Laminin receptors

Laminin receptors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

MSH receptors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT P-glycoproteins

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Prostate-specific antigen

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Somatostatin receptors

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Biopolymers

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Anthracyclines

Radionuclides, biological studies

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic

use); BIOL (Biological study); PROC (Process); USES (Uses)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Antigens

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(neoantigens; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Receptors

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(nitrobenzylthioinosine-binding; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Transport proteins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(norepinephrine-transporting; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Benzodiazepine receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(peripheral; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Drug delivery systems

(prodrugs; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Proliferation inhibition

(proliferation inhibitors; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Ligands

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC

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(Process)
        (targetable; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
IT
     Drug delivery systems
        (targeted; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
IT
     Nucleosides, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (transport proteins; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
IT
     Antigens
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (tumor-assocd.; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
IT
     Vaccines
        (tumor; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
IT
     Biological transport
        (uptake; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
IT
     Antitumor agents
        (vaccines; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
TΤ
     Opioid receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (.sigma.-opioid; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
IT
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (.alpha.v.beta.3; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
TT
     9001-01-8, Kallikrein
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (2, human glandular; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
ፕ ፕ
     9024-62-8, Orotidine 5'-phosphate decarboxylase
                                                       9029-03-2, Dihydroorotic
                          9032-02-4
     acid dehydrogenase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
TT
     342397-39-1F
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PEP (Physical, engineering
     or chemical process); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
IT
     23214-92-8DP, immucillin G derivs.
                                          209799-75-7DP, doxorubicin derivs.
                                   341549-71-1P
                                                  341549-87-9P
                    341549-53-9P
     341549-52-8P
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                                   342397-65-3P
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                    342397-18-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PNU (Preparation, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
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                    341549-27-7P
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IT
     341549-26-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
                               9001-77-8
                                          9001-92-7, proteinase
IT
     9001-12-1, collagenase
     trypsin 9004-06-2, Elastase 9004-08-4, cathepsin
                                                             9025-26-7,
                                                  9030-23-3, Thymidine
     cathepsin d
                  9025-62-1, Steroid sulfatase
                                                         9039-53-6, urokinase
                     9031-61-2, Thymidylate synthase
     phosphorylase
     9040-48-6, Gelatinase 9045-77-6, Fatty acid synthase
                                                                9047-22-7.
                   9074-87-7, glutamate carboxypeptidase II
                                                                60616-82-2,
     cathepsin b
     cathepsin L
                   62229-50-9, Egf
                                     79955-99-0, Stromelysin 1
                                                                   84419-03-4,
                           94716-09-3, cathepsin k
                                                       115926-52-8,
     quanidinobenzoatase
     Phosphatidylinositol 3-kinase 141256-52-2, matrilysin 141907-41-7,
     matrix metalloproteinase 142008-29-5, Protein kinase a 142243-02-5, Map kinase 142805-58-1, Map kinase kinase 145267-01-2, stromelysin 3
     146480-35-5, Gelatinase A 162032-86-2, cathepsin O 175449-82-8, Collagenase 3 241475-96-7, Matriptase
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
IΤ
     9001-90-5, plasmin
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
     50-07-7, Mitomycin c 57-22-7, Vincristine 58-85-5D, Biotin, masked derivs. 59-30-3D, Folic acid, masked derivs. 518-28-5D,
IT
     Podophyllotoxin, derivs.
                                 519-23-3D, Ellipticine, derivs.
                  7689-03-4, Camptothecin 10159-53-2D, Phosphoramide
     Vinblastine
     mustard, analogs 11116-31-7D, Bleomycin A2, derivs. 24280-93-1,
     Mycophenolic acid 33069-62-4D, Taxol, derivs. 52128-35-5, Trimetrexate
     65271-80-9D, Mitoxantrone, derivs. 77327-05-0, Didemnin B 112953-11-4
     114899-77-3D, Ecteinascidin 743, derivs. 124689-65-2D, analogs
     139987-54-5, BW 1843U89
                               175795-76-3 236743-94-5, Phthalascidin
     265646-19-3, Indanocine
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
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RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic
use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
   (multifunctional delivery vehicles for selective cellular targeting of
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    RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic
    use); BIOL (Biological study); PREP (Preparation); RACT
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                                                                 341549-83-5P
     341549-79-9P
                    341549-80-2P
                    341549-85-7P
                                   341549-86-8P
     341549-84-6P
     RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
IT
              2495-35-4
                           3326-32-7
                                       3588-30-5
                                                   110914-51-7
                                                                 121031-01-4
     51-67-2
                   341549-28-8 341549-30-2 341549-33-5
                                                            341549-39-1
     178623-11-5
     341549-73-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
                 173039-08-2P
                                 341549-29-9P
                                                341549-31-3P
                                                               341549-32-4P
IT
     5621-44-3P
                    341549-36-8P
                                                  341549-38-0P
                                                                 341549-40-4P
     341549-34-6P
                                   341549-37-9P
                    341549-70-0P
     341549-69-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (multifunctional delivery vehicles for sel ctive cellular targeting of
        drugs)
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341549-72-2P
ΙT
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
                                                341549-44-8
                                                              341549-45-9
     341549-41-5
                   341549-42-6
                                 341549-43-7
                                                341549-49-3
                                                              341549-50-6
                                 341549-48-2
                   341549-47-1
     341549-46-0
                                                              341549-67-5
     341549-51-7
                   341549-64-2
                                 341549-65-3
                                                341549-66-4
     341549-68-6
                   341549-77-7
                                 341990-71-4
                                                342392-74-9
                                                              342393-39-9
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
TT
     9001-78-9, Alkaline phosphatase
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (placental type; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
     38048-32-7
IΤ
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (receptors; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
     341549-52-8P 341552-87-2P 341553-15-9P
TT
     341553-47-7P 341553-59-1P 341990-94-1P
     341990-96-3P 341990-98-5P 341990-99-6P
     341991-00-2P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PNU (Preparation, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
RN
     341549-52-8 HCAPLUS
CN
     Butanedioic acid, [[5-[[[[4-(3S,19S)-19-amino-38-[2-[[(2R)-2-18]])]]]]
     (acetylamino)-3-(dimethylamino)-3-oxopropyl]dithio]-5-[[[[[(2E)-2,3-
     dihydro-2-[(4-hydroxy-3,5-dimethylphenyl)methylene]-5,6-dimethoxy-1-oxo-1H-
     inden-7-yl]amino]carbonyl]oxy]methyl]phenyl]-3-[(9H-fluoren-9-
     ylmethoxy) carbonyl]-1, 6, 17, 20, 34-pentaoxo-10, 13, 24, 27, 30, 36-hexaoxa-
     2,7,16,21,33-pentaazaoctatriacont-1-yl]phenyl][(2-amino-1,4-dihydro-4-oxo-
     6-pteridinyl)methyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-
     dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester
     (9CI)
           (CA INDEX NAME)
```

Absolute stereochemistry. Double bond geometry as shown.

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RN 341552-87-2 HCAPLUS

9,12,22,25,28,31,41-Heptaoxa-2,6,15,19,34,38,44-heptaaza-48phosphadopentacontane-3,50,52-tricarboxylic acid, 1-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[(3-carboxy-1-oxopropoxy)methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-18-[18-[7-[[[[2-(1,3-dicarboxypropyl)-2,3-dihydro-1-oxo-1H-isoindol-5-yl][(1,2-dihydro-3-methyl-1-oxobenzo[f]quinazolin-9-yl)methyl]amino]carbonyl]oxy]methyl]-5,8-dihydro-5,8-dioxo-2-naphthalenyl]-1,14-dioxo-5,8,11-trioxa-2,15-diazaoctadec-1-yl]-35-(1,14-dioxo-5,8,11-trioxa-2,15-diazadocos-1-yl)-48-hydroxy-1,5,16,20,33,37,45-heptaoxo-,48-oxide,(3S,18S,35S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

NH2

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P HO O PAGE 2-A

V V

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Me \_\_\_\_\_

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RN 341553-15-9 HCAPLUS

11,14,24,27,30,33,43,46,49-Nonaoxa-2,7,17,21,36,40,52-heptaaza-56-phosphahexacontane-3,58,60-tricarboxylic acid, 1-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[((3-carboxy-1-oxopropoxy)methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-20-[17-[6-[[[[(2-(1,3-dicarboxypropyl)-2,3-dihydro-1-oxo-1H-isoindol-5-yl][(1,2-dihydro-3-methyl-1-oxobenzo[f]quinazolin-9-yl)methyl]amino]carbonyl]oxy]methyl]-5,8-dihydro-5,8-dioxo-1-naphthalenyl]-1,14-dioxo-5,8,11-trioxa-2,15-diazaheptadec-1-yl]-37-(1,14-dioxo-5,8,11-trioxa-2,15-diazadocos-1-yl)-56-hydroxy-1,6,18,22,35,39,53-heptaoxo-,56-oxide, (3S,20S,37S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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H2N----

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RN 341553-47-7 HCAPLUS
CN 10,13,16,26,29,32,35,45,48,51-Decaoxa-2,7,19,23,42,54-hexaaza-58-phosphadohexacontane-3,60,62-tricarboxylic acid, 1-[4-[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[(3-carboxy-1-oxopropoxy)methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-22-[17-[6-[[[[1-[5-(5-carboxy-3-methyl-2-pentenyl)-1,3-dihydro-6-methoxy-7-methyl-3-oxo-4-isobenzofuranyl]oxy]-2,2,2-trifluoroethyl]amino]carbonyl]oxy]methyl]-5,8-dioxo-1-naphthalenyl]-1,14-dioxo-5,8,11-trioxa-2,15-diazaheptadec-1-yl]-39-(1,14-dioxo-5,8,11-trioxa-2,15-diazadocos-1-yl)-58-hydroxy-1,6,20,24,37,41,55-heptaoxo-,58-oxide, (3S,22S,39S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

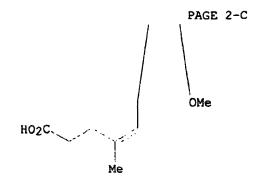
Double bond geometry unknown.

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(CH<sub>2</sub>) 6



RN 341553-59-1 HCAPLUS

Quinolinium, 1-[[[7-[((21S,38S)-21-[(16S)-18-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl] [[[3-[((3-carboxy-1-oxopropoxy)methoxy]carbonyl]-4-[((2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-16-carboxy-2,13,18-trioxo-6,9-dioxa-3,12,17-triazaoctadec-1-yl]-59,61-dicarboxy-38-(1,14-dioxo-5,8,11-trioxa-2,15-diazadocos-1-yl)-57-hydroxy-57-oxido-2,7,20,23,36,40,54-heptaoxo-10,13,16,25,28,31,34,44,47,50-decaoxa-3,6,19,22,37,41,53-heptaaza-57-phosphahenhexacont-1-yl]dithio]-8-[(carboxymethyl)dithio]-1,5-dihydro-3-oxido-2,4,3-benzodioxaphosphepin-3-yl]oxy]methyl]-4-carboxy-6-fluoro-2-(2'-fluoro-[1,1'-biphenyl]-4-yl)-3-methyl-, chloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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RN 341990-94-1 HCAPLUS

L-Alaninamide, N-[41-[2',3'-O-[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[2-oxido-5-(phosphonoxy)-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methylene]-N-[(4-nitrophenyl)methyl]-5'-thioadenosin-5'-S-yl]-27-[14-[2',3'-O-[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[2-oxido-5-(phosphonooxy)-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methylene]-N-[(4-nitrophenyl)methyl]-5'-thioadenosin-5'-S-yl]-11-oxo-3,6,9-trioxa-12-azatetradec-1-yl]-1,13,26,38-tetraoxo-12-(11-oxo-3,6,9-trioxa-12-azanonadec-1-yl)-3,6,9,15,18,21,24,30,33,36-decaoxa-12,27,39-triazahentetracont-1-yl]-D-seryl-N-[1-(aminoiminomethyl)-2-hydroxy-3-piperidinyl]- (9CI) (CA INDEX NAME)

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RN 341990-96-3 HCAPLUS

L-Glutamic acid, N-[[5-[2-[2-amino-8-[[[3-[18-[(16S)-18-[4-[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl] [[[3-[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[2-oxido-5-(phosphonooxy)-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]amino]phenyl]-16-carboxy-13,18-dioxo-3,6,9-trioxa-12,17-diazaoctadec-1-yl]-48-[4-[(4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-33-[15-[4-[(4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-13-oxo-3,6,9-trioxa-12-azapentadec-1-yl]-5,19,32,46-tetraoxo-3,9,12,15,21,24,27,30,36,39,42-undecaoxa-6,18,33,45-tetraazaoctatetracont-1-yl]-4-[[(2R)-2-amino-3-oxo-3-[[(phosphonooxy)methyl]amino]propyl]dithio]phenyl]methoxy]carbonyl]-4,6,7,8-tetrahydro-4-oxo-1H-pyrimido[5,4-b][1,4]thiazin-6-yl]ethyl]-3-thienyl]carbonyl]- (9CI) (CA INDEX NAME)

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RN 341990-98-5 HCAPLUS
7,10,13,19,22,25,28,34,37,40-Decaoxa-4,16,31,43-tetraazaoctatetracontan-48-oic acid, 47-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]][[[3-[(2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[5-(phosphonooxy)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]amino]benzoyl]amino]-31-[17-[5-[[[(2S,3S,4R,5R)-2-(2-amino-4,5-dihydro-4-oxo-1H-pyrrolo[3,2-d]pyrimidin-7-yl)-3,4-dihydroxy-5-(2-phosphonoethyl)-1-pyrrolidinyl]carbonyl]oxy]methyl]-2-[[(2S)-2-amino-3-oxo-3-[[2-(phosphonooxy)ethyl]amino]propyl]thio]phenyl]-13-oxo-3,6,9,15-tetraoxa-12-azaheptadec-1-yl]-1-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-16-[15-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]-2H-pyran-2-yl]-13-oxo-3,6,9-trioxa-12-azapentadec-1-yl]-3,17,30,44-tetraoxo-,(47S)-(9CI) (CA INDEX NAME)

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RN 341990-99-6 HCAPLUS
7,10,13,19,22,25,28,34,37,40-Decaoxa-4,16,31,43-tetraazaoctatetracontan-48-oic acid, 47-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]][[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[5-(phosphonooxy)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]amino]benzoyl]amino]-31-[14-[[3-[(2R,3R,4S,5S)-5-(2-amino-4,5-dihydro-4-oxo-1H-pyrrolo[3,2-d]pyrimidin-7-yl)-3,4-dihydroxy-2-pyrrolidinyl]methoxy]-8-[(carboxymethyl)dithio]-1,5-dihydro-3-oxido-2,4,3-benzodioxaphosphepin-7-yl]dithio]-13-oxo-3,6,9-trioxa-12-azatetradec-1-yl]-1-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]-2H-pyran-2-yl]-16-[15-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-13-oxo-3,6,9-trioxa-12-azapentadec-1-yl]-3,17,30,44-tetraoxo-, (47S)- (9CI) (CA INDEX NAME)

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RN 341991-00-2 HCAPLUS

Uridine, 5'-0-[7-[[15-[(16S)-18-[4-[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl] [[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[2-oxido-5-(phosphonooxy)-1,3;2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]amino]phenyl]-16-carboxy-13,18-dioxo-3,6,9-trioxa-12,17-diazaoctadec-1-yl]-45-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-30-[15-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-13-oxo-3,6,9-trioxa-12-azapentadec-1-yl]-2,16,29,43-tetraoxo-6,9,12,18,21,24,27,33,36,39-decaoxa-3,15,30,42-tetraazapentatetracont-1-yl]dithio]-8-[(carboxymethyl)dithio]-1,5-dihydro-3-oxido-2,4,3-benzodioxaphosphepin-3-yl]-5,6-dihydro-6-oxo-(9CI) (CA INDEX NAME)

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341549-95-9P 341550-24-1P 341550-66-1P
TΤ
     341550-72-9P 341550-74-1P 341550-93-4P
     341550-94-5P 341550-95-6P 341550-97-8P
     341551-63-1P 341551-64-2P 341551-74-4P
     341551-88-0P 341551-93-7P 341552-52-1P
     341552-53-2P 341552-54-3P 341552-96-3P
     341553-21-7P 341553-23-9P 341553-26-2P
     341553-28-4P 341553-29-5P 341553-30-8P
     341553-32-0P 341553-33-1P 341553-36-4P
     341553-43-3P 341553-48-8P 341553-50-2P
     341990-82-7P 341990-83-8P 341990-84-9P
     341990-85-0P 341990-86-1P 341990-87-2P
     341990-95-2P 341990-97-4P
     RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
RN
     341549-95-9 HCAPLUS
     Butanedioic acid, [[5-[[[[(2-amino-1,4-dihydro-4-oxo-6-
CN
     pteridinyl)methyl][4-[(3S)-3-carboxy-33-[2-[[(2R)-10-(9H-fluoren-9-yl)-8-
     (9H-fluoren-9-ylmethoxy)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-8-oxido-3-oxo-7,9-dioxa-4-aza-8-phosphadec-1-yl]dithio]-5-[[[[[3-[[3-[(9-
     methoxy-5,11-dimethyl-6H-pyrido[4,3-b]carbazol-1-
     ylaminopropylmethylaminopropylaminocarbonyloxymethylphenyl-
     1,6,29-trioxo-10,13,16,22,25,31-hexaoxa-2,7,19,28-tetraazatritriacont-1-
     yl]phenyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-
     yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX
     NAME)
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O CO2H

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RN 341550-24-1 HCAPLUS

5,11,14,20,23,26-Hexaoxa-2,8,17,29-tetraazatetratriacontanedioic acid,
33-[[4-[[(7-amino-1,5-dihydro-5-oxopyrido[3,4-b]pyrazin-3-yl)methyl][[[3-[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]benzo
yl]amino]-2-[2-[[3-(dimethylamino)-3-oxopropyl]dithio]phenyl]-7,30-dioxo-,
34-(9H-fluoren-9-ylmethyl) 1-[2-oxo-2-[(2S,4S)-2,5,12-tris[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-1,2,3,4,6,11-hexahydro-7-methoxy-6,11-dioxo-4[[2,3,6-trideoxy-3-(2,3-dihydro-1H-pyrrol-1-yl)-4-0-[(9H-fluoren-9-ylmethoxy)carbonyl]-.alpha.-L-lyxo-hexopyranosyl]oxy]-2naphthacenyl]ethyl] ester (9CI) (CA INDEX NAME)

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` NMe2

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RN 341550-66-1 HCAPLUS

CN 5,8-Dioxa-2,11-diazahexadecanedioic acid, 15-[[[5-[2-[2-amino-8-[[[3-[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]-4,6,7,8-tetrahydro-4-oxo-1H-pyrimido[5,4-b][1,4]thiazin-6-yl]ethyl]-2-thienyl]carbonyl]amino]-12-oxo-, 1-[[4-[[4-[[[(2S,3S,4R,5R)-2-(2-amino-4,5-dihydro-4-oxo-1H-pyrrolo[3,2-d]pyrimidin-7-yl)-5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]methyl]-3,4-bis[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-1-pyrrolidinyl]carbonyl]oxy]methyl]phenyl]dithio]-3-[24-carboxy-12-[[(1,1-dioxidobenzo[b]thien-2-yl)methoxy]carbonyl]-5-oxo-3,9,15,18-tetraoxa-21,22-dithia-6,12-diazatetracos-1-yl]phenyl]methyl]
16-(9H-fluoren-9-ylmethyl) ester, (15S)- (9CI) (CA INDEX NAME)

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RN 341550-72-9 HCAPLUS

5,8-Dioxa-2,11-diazahexadecanedioic acid, 15-[[[5-[2-[2-amino-8-[[[3-[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]-4,6,7,8-tetrahydro-4-oxo-1H-pyrimido[5,4-b][1,4]thiazin-6-yl]ethyl]-2-thienyl]carbonyl]amino]-12-oxo-, 1-[[4-[[4-[[[(2S,3S,4R,5R)-2-(2-amino-4,5-dihydro-4-oxo-1H-pyrrolo[3,2-d]pyrimidin-7-yl)-5-[[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]methyl]-3,4-bis[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-1-pyrrolidinyl]carbonyl]oxy]methyl]phenyl]dithio]-3-[2-(carboxymethoxy)ethyl]phenyl]methyl] 16-[9H-fluoren-9-ylmethyl)ester, (15S)- (9CI) (CA INDEX NAME)

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KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

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RN 341550-74-1 HCAPLUS

CN Butanedioic acid, [[5-{[[[2-amino-6-[2-[5-[[[(1S)-4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1-[(9H-fluoren-9-ylmethoxy)carbonyl]-4-oxobutyl]amino]carbonyl]-2-thienyl]ethyl]-1,4,6,7-tetrahydro-4-oxo-8H-pyrimido[5,4-b][1,4]thiazin-8-yl]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester

Absolute stereochemistry.

(9CI) (CA INDEX NAME)

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RN 341550-93-4 HCAPLUS
CN Butanedioic acid, [[5-[[(chlorocarbonyl)oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

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RN 341550-94-5 HCAPLUS

Butanedioic acid, [[5-[[[6-[2-(5-carboxy-2-thienyl)ethyl]-2-[[(1,1-dimethylethyl)diphenylsilyl)amino]-1,4,6,7-tetrahydro-4-oxo-8H-pyrimido[5,4-b][1,4]thiazin-8-yl]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME) CN

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RN 341550-95-6 HCAPLUS

CN Butanedioic acid, [[5-[[[[2-amino-6-[2-(5-carboxy-2-thienyl)ethyl]-1,4,6,7-tetrahydro-4-oxo-8H-pyrimido[5,4-b][1,4]thiazin-8-yl]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

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RN 341550-97-8 HCAPLUS

L-Glutamic acid, N-[[5-[2-[2-amino-8-[[[3-[[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]-4,6,7,8-tetrahydro-4-oxo-1H-pyrimido[5,4-b][1,4]thiazin-6-yl]ethyl]-2-thienyl]carbonyl}-, 1-(9H-fluoren-9-ylmethyl)ester (9CI) (CA INDEX NAME) CN

RN 341551-63-1 HCAPLUS
CN Butanedioic acid, 9H-fluoren-9-ylmethyl [{5-(hydroxymethyl)-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl ester (9CI) (CA INDEX NAME)

PAGE 2-A

RN 341551-64-2 HCAPLUS CN

Butanedioic acid, 9H-fluoren-9-ylmethyl [[5-formyl-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl ester (9CI) (CA INDEX NAME)

PAGE 2-A

RN

341551-74-4 HCAPLUS
L-Glutamic acid, N-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[(2-dimethylamino)-2-oxoethoxy] CN oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]benzo yl]-, 1-(9H-fluoren-9-ylmethyl) ester (9CI) (CA INDEX NAME)

PAGE 1-B

RN

341551-88-0 HCAPLUS
3,6,10,15-Tetraoxa-7,9-diphosphaoctadecanoic acid, 7-[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]-14-(2,2-dimethyl-1-oxopropoxy)-13,17,17-trimethyl-16-oxo-9-[2-[(trifluoroacetyl)amino]ethoxy]-, 7,9-dioxide (9CI) (CA INDEX CN NAME)

RN 341551-93-7 HCAPLUS

CN Benzoic acid, 5-(hydroxymethyl)-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

RN 341552-52-1 HCAPLUS

CN Benzoic acid, 5-[[(chlorocarbonyl)oxy]methyl]-2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

RN 341552-53-2 HCAPLUS

CN Benzoic acid, 2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-(hydroxymethyl)-, 2-(dimethylamino)-2-

oxoethyl ester (9CI) (CA INDEX NAME)

RN 341552-54-3 HCAPLUS

CN Benzoic acid, 2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-formyl-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

RN 341552-96-3 HCAPLUS

CN 11,14,17,27,30,33,36,46,49,52-Decaoxa-2,7,20,24,39,43,55-heptaaza-59-phosphatrihexacontane-3,61,63-tricarboxylic acid, 1-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-23-(13-carboxy-1-oxo-5,8,11-trioxa-2-azatridec-1-yl)-40-(1,14-dioxo-5,8,11-trioxa-2,15-diazanonadec-1-yl)-59-(9H-fluoren-9-ylmethoxy)-1,6,21,25,38,42,56-heptaoxo-,3,61,63-tris(9H-fluoren-9-ylmethyl) ester, 59-oxide, (3S,23S,40S)-(9CI) (CA INDEX NAME)

PAGE 1-B

NHBu-n

PAGE 1-D

PAGE 2-E

RN 341553-21-7 HCAPLUS

2,4,10-Trioxa-7,12-diaza-3-phosphatridecan-13-oic acid,
7-[6-[[2-(2-aminoethoxy)ethyl][2-[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]ethyl]amino]-4,8-di-1-piperidinylpyrimido[5,4-d]pyrimidin-2-yl]-1-(9H-fluoren-9-yl)-3-(9H-fluoren-9-ylmethoxy)-11-(trifluoromethyl)-, [4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-

oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2oxo thoxy]carbonyl]phenyl]methyl ester, 3-oxide (9CI) (CA INDEX NAME)

## PAGE 1-A

### PAGE 1-B

RN 341553-23-9 HCAPLUS
CN Benzoic acid, 2-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido1,3,2-dioxaphosphorinan-2-yl]oxy]-5-[[[[(1-chloro-2,2,2trifluoroethyl)amino]carbonyl]oxy]methyl]-, 2-(dimethylamino)-2-oxoethyl
ester (9CI) (CA INDEX NAME)

RN 341553-26-2 HCAPLUS

CN 1H-1,4-Diazepinium, 1-[3-[[4-[2-(2-aminoethoxy)ethoxy]-3,5-dimethoxybenzoyl]amino]propyl]-1-[[1-[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]methyl]hexahydro-4-[4-[(3,4,5-trimethoxybenzoyl)amino]butyl]- (9CI) (CA INDEX NAME)

PAGE 1-B

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PAGE 2-B

RN 341553-28-4 HCAPLUS

CN Benzoic acid, 2-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-[[[((2,2,2-trifluoro-1hydroxyethyl)amino]carbonyl]oxy]methyl]-, 3-methyl-2-oxobutyl ester (9CI) (CA INDEX NAME)

RN 341553-29-5 HCAPLUS

CN 1H-1,4-Diazepinium, 1-[[1-[[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroacetyl)amino]phenyl]hexahydro-4-(trifluoroacetyl)-1-[3-(trifluoroacetyl)amino]propyl]- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 341553-30-8 HCAPLUS CN

1H-1,4-Diazepinium, 1-(3-aminopropyl)-1-[[1-[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]methyl]hexahydro- (9CI) (CA INDEX NAME)

### PAGE 1-B

RN 341553-32-0 HCAPLUS

CN 1H-1,4-Diazepinium, 1-[[1-[[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]methyl]-1-[3-[[3,5-dimethoxy-4-[2-[2-[[(2-

propenyloxy)carbonyl]amino]ethoxy]ethoxy]benzoyl]amino]propyl]hexahydro-(9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-B

OMe

RN 341553-33-1 HCAPLUS

CN 1H-1,4-Diazepinium, 1-[[1-[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]methyl]-1-[3-[[3,5-dimethoxy-4-[2-[2-[[(2-propenyloxy)carbonyl]amino]ethoxy]ethoxy]benzoyl]amino]propyl]hexahydro-4-[3-[(3,4,5-trimethoxybenzoyl)amino]propyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

$$H_2C = CH - CH_2 - O - C - NH - CH_2 - CH_2 - O - CH_2$$

PAGE 2-B

RN 341553-36-4 HCAPLUS

CN Butanedioic acid, mono[[[5-[[[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]{4-[(3S)-36-[5-[[[[(2,4-diamino-5-methyl-6-quinazolinyl)methyl](3,4,5-trimethoxyphenyl)amino]carbonyl]oxy]methyl]-2-[[(2R)-10-(9H-fluoren-9-yl)-8-(9H-fluoren-9-ylmethoxy)-2-[((9H-fluoren-9-ylmethoxy)carbonyl]amino]-8-oxido-3-oxo-7,9-dioxa-4-aza-8-phosphadec-1-

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

'yl]dithio]phenyl]-3-[(9H-fluor n-9-ylmethoxy)carbonyl]-1,6,32-trioxo-10,13,16,22,25,28,34-heptaoxa-2,7,19,31-tetraazahexatriacont-1-yl]phenyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl] ester (9CI) (CA INDEX NAME)

### PAGE 1-A

### PAGE 2-A

PAGE 5-A

PAGE 6-A

PAGE 6-B

 $-cH_2-co_2H$ 

RN 341553-43-3 HCAPLUS

Benzoic acid, 2-[[5-{[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy}-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-[{(chlorocarbonyl)oxy]methyl}-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME) CN

RN 341553-48-8 HCAPLUS

CN Butanedioic acid, [[5-[[[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][4-[(3S,19S)-19-amino-3-[(9H-fluoren-9-ylmethoxy)carbonyl]-36-[6-[[[[[1-[[5-[6-(9H-fluoren-9-ylmethoxy)-3-methyl-6-oxo-2-hexenyl]-1,3-dihydro-6-methoxy-7-methyl-3-oxo-4-isobenzofuranyl]oxy]-2,2,2-trifluoroethyl]amino]carbonyl]oxy]methyl]-5,8-dihydro-5,8-dioxo-1-naphthalenyl]-1,6,17,20,33-pentaoxo-10,13,24,27,30-pentaoxa-2,7,16,21,34-pentaozahexatriacont-1-yl]phenyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

PAGE 1-B

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

PAGE 1-D

PAGE 2-B

RN 341553-50-2 HCAPLUS

8,11-Dioxa-1,5,14,19-tetraazaeicosane-1,2,18-tricarboxylic acid,
20-[4-[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[3-[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-4,15,20-trioxo-, 1-(1-[1,1'-biphenyl]-4-yl-1-methylethyl) 18-(9H-fluoren-9-ylmethyl) ester, (2S,18S)- (9CI) (CA INDEX NAME)

PAGE 1-C

PAGE 2-A

RN 341990-82-7 HCAPLUS

L-Phenylalanine, N-[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]phenyl]methoxy]carbonyl]-N-[[(4-methoxyphenyl)amino]carbonyl]-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

PAGE 2-A

RN 341990-83-8 HCAPLUS

L-Phenylalanine, N-[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]phenyl]methoxy]carbonyl]-N-[[(4-methoxyphenyl)amino]carbonyl]-L-methionyl-L-leucyl-, 2,2,2-trichloroethylester (9CI) (CA INDEX NAME)

PAGE 2-A

RN 341990-84-9 HCAPLUS

L-Phenylalanine, N-[[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]-N-[[(4-methoxyphenyl)amino]carbonyl]-L-methionyl-L-leucyl-, 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME) CN

RN 341990-85-0 HCAPLUS
CN Benzoic acid, 5-[[[[(1S)-1-carboxy-3-(methylthio)propyl][[(4methoxyphenyl)amino]carbonyl]amino]carbonyl]oxy]methyl]-2-[[5-[[(1,1dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy], 1-[2-(dimethylamino)-2-oxoethyl] ester (9CI) (CA INDEX NAME)

### Absolute stereochemistry.

RN 341990-86-1 HCAPLUS
CN Benzoic acid, 5-[[[[(1S)-1-[(1-[1,1'-biphenyl]-4-yl-1 methylethoxy)carbonyl]-3-(methylthio)propyl][[(4 methoxyphenyl)amino]carbonyl]amino]carbonyl]oxy]methyl]-2-[[5-[[(1,1 dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy] , 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

# PAGE 2-A

RN 341990-87-2 HCAPLUS

CN Benzoic acid, 5-[[[[(1S)-1-[(1-[1,1'-biphenyl]-4-yl-1-methylethoxy)carbonyl]-3-(methylthio)propyl]amino]carbonyl]oxy]methyl]-2[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2dioxaphosphorinan-2-yl]oxy]-, 2-(dimethylamino)-2-oxoethyl ester (9CI)
(CA INDEX NAME)

PAGE 1-B

CN

RN

341990-95-2 HCAPLUS
Adenosine, 5'-S-(2-aminoethyl)-2',3'-O-[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]phenyl]methylene]-N-[(4-nitrophenyl)methyl]-5'-thio- (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

RN 341990-97-4 HCAPLUS

CN L-Glutamic acid, N-[4-[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]phenyl]methoxy]carbonyl]amino]benzoyl]-, 1-(9H-fluoren-9-ylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

IT 341549-55-1P

RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (multifunctional delivery vehicles for selective cellular targeting of drugs)

RN 341549-55-1 HCAPLUS

CN L-Glutamic acid, N-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[(3-[[(4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]benzoyl]-, 1-(9H-fluoren-9-ylmethyl)ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2003 ACS
      2001:185764 HCAPLUS
AN
DN
      134:237345
TI
      Preparation of prodrugs for liver specific drug delivery
      Erion, Mark D.; Reddy, K. Raja
IN
PA
      Metabasis Therapeutics, Inc., USA
      PCT Int. Appl., 160 pp.
      CODEN: PIXXD2
DT
      Patent
LA
      English
IC
      ICM C07F009-6584
      ICS C07F009-6571; C07H015-26; C07H015-252; A61K031-66; A61K031-70;
           A61P031-00; A61P035-00
CC
      26-1 (Biomolecules and Their Synthetic Analogs)
      Section cross-reference(s): 1, 9, 63
FAN. CNT 1
      PATENT NO.
                          KIND DATE
                                                   APPLICATION NO.
                                                                        DATE
PΙ
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                          A1
                                 20010315
                                                   WO 2000-US24693 20000908
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           RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
               DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

A1 20020605 EP 2000-961694 20000908
      EP 1210354
           R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL
PRAI US 1999-153128P
                           Ρ
                                 19990908
      WO 2000-US24693
                           W
                                 20000908
os
      MARPAT 134:237345
GI
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Cyclic phosph(oramid)ate prodrugs, such as I [M = pharmaceutical agent, such as camptothecin, paclitaxel, etc.; V, W, W' = H, alkyl, arylalkyl,AB aryl, heteroaryl, alkenyl, alkynyl, etc.; Z = H, hydroxymethyl, acyloxymethyl, etc.; VZ or VW = fused cyclic group; Y = O, NR, etc.; R = H, alkyl, etc.], were prepd. and formulated for pharmaceutical use for the delivery of drugs. Thus, prodrug II was prepd. in 48% yield from 1-(4-pyridyl)-1,3-propanediol, POCl3, and etoposide. The prepd. prodrugs were tested for their resp. biol. activities, such as II being tested for activation in rat hepatocytes. The proposed uses of the prodrugs are to treat diseases that benefit from enhanced drug distribution to the liver and like tissues and cells that express cytochrome P 450, including hepatitis, cancer, liver fibrosis, malaria, other viral and parasitic infections, and metabolic diseases where the liver is responsible for the overprodn. of the biochem. end product, e.g. glucose (diabetes); cholesterol, fatty acids and triglycerides (hyperlipidemia) (atherosclerosis) (obesity). These prodrugs are designed to enhance oral drug delivery, to prolong pharmacodynamic half-life of the drug, to achieve sustained delivery of the parent drug, to increase the therapeutic index of the drug, and to be useful in the delivery of diagnostic imaging agents to the liver.

II

ST cyclic phosphate prodrug prepn; phosphoramide cyclic prodrug prepn; liver treatment cyclic phosphate prodrug prepn

IT Drug delivery systems

TT

IT

IT

(prodrugs; prepn. of prodrugs for liver specific drug delivery)

329325-41-9P 329325-43-1P 329325-44-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(prepn. of prodrugs for liver specific drug delivery)

IT 104-55-2 2629-72-3, 4-Pyridinepropanol 4704-94-3 4799-68-2

50409-12-6 104196-23-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of prodrugs for liver specific drug delivery)

19790-60-4P 90533-81-6P 329325-40-8P, 1-(4-Pyridyl)-1,3-propanediol 329325-42-0P 329325-45-3P 329325-46-4P 329325-47-5P 329361-60-6P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of prodrugs for liver specific drug delivery) 1404-00-8, Mitomycin 7689-03-4, Camptothecin 9014-02-2,

```
Neocarzinostatin 11033-22-0, Coformycin 20830-81-3, Daunorubicin 24280-93-1, Mycophenolic acid 25316-40-9, Doxorubicin hydrochlorid
    29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide
    53910-25-1, Deoxycoformycin 56420-45-2, Epirubicin
                                                            58957-92-9,
    Idarubicin 65271-80-9, Mitoxantrone 70052-12-9, Eflornithine
                              88303-60-0, Losoxantrone
                                                          91421-43-1,
    72496-41-4, Pirarubicin
                          91441-23-5, Piroxantrone
                                                      97682-44-5, Irinotecan
    9-Aminocamptothecin
                                                       114977-28-5, Docetaxel
                          114797-28-3, Esperamicin
    105760-98-3, NK 611
    117048-59-6, Combretastatin A-4 123948-87-8, Topotecan 127882-73-9, GL
           129564-92-7, Azatoxin 149882-10-0, Lurtotecan 155233-45-7
    331
                             213313-16-7, Combretastatin A-4 (S,S)-dioxolane
    169869-90-3, DX 8951F
     RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT
     (Reactant or reagent); USES (Uses)
        (prepn. of prodrugs for liver specific drug delivery)
              THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE
(1) Bedford, S; Bioorganic & Medicinal Chemistry Letters 1996, V6(2), P157
    HCAPLUS
(2) Bristol-Myers Squibb Co; EP 0481214 A 1992 HCAPLUS
(3) Metabasis Therapeutics; WO 9839342 A 1998 HCAPLUS
(4) Metabasis Therapeutics; WO 9839343 A 1998 HCAPLUS
(5) Metabasis Therapeutics; WO 9839344 A 1998 HCAPLUS
(6) Metabasis Therapeutics; WO 9945016 A 1999 HCAPLUS
     329325-41-9P 329325-44-2P
ΙT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of prodrugs for liver specific drug delivery)
     329325-41-9 HCAPLUS
RN
     Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5-[3,5-dimethoxy-4-
CN
     [[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]-9-[[4,6-
     O-(1R)-ethylidene-.beta.-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-,
     (5R, 5aR, 8aR, 9S) - (9CI) (CA INDEX NAME)
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Absolute stereochemistry.

### PAGE 1-A

## PAGE 2-A

RN

CN

329325-44-2 HCAPLUS
1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione,
4-ethyl-4-[{2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy}-,
(4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2003 ACS
L24
     2000:706969 HCAPLUS
AN
     133:261536
DN
     Pharmaceutical compositions comprising cyclic glycerophosphates and
TI
     analogs thereof for promoting neural cell differentiation
IN
     Shinitzky, Meir
     Yeda Research and Development Co. Ltd., Israel
PA
     PCT Int. Appl., 42 pp.
50
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61K031-00
     1-11 (Pharmacology)
     Section cross-reference(s): 29, 63
FAN.CNT 1
                                             APPLICATION NO.
                                                               DATE
                       KIND DATE
     PATENT NO.
                                             WO 2000-IL185
                                                               20000324
                              20001005
     WO 2000057865
                        A2
PΙ
     WO 2000057865
                        A3
                              20010628
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, K2, LC, LK, LR, LS, LT, LU,
                                       MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             LV, MA, MD, MG, MK, MN,
              SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
              ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
                                           SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
         RW: GH, GM, KE, LS, MW, SD, SL,
              DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
              CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                                                20000324
                              20011218
                                             BR 2000-9296
     BR 2000009296
                        Α
                                                               20000324
                                             EP 2000-912877
                              20011219
     EP 1162959
                        A2
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT,
                          LV, FI, RO
                                                                20000324
                                              JP 2000-607616
     JP 2002540146
                        T2
                              20021126
                              19990325
PRAI IL 1999-129178
                        Α
                              20000324
     WO 2000-IL185
     MARPAT 133:261536
OS
     Cyclic glycerophosphates and analogs thereof (CGs) are shown to exert neural promoting activities in target cells. Such activities include
AB
     promotion of neuronal outgrowth, promotion of nerve growth, provision of
     dopaminotrophic supporting environment in a diseased portion of the brain,
     prevention of nerve degeneration and nerve rescue. These activities of
     the CGs render them useful for treatment of various disorders including
     but not limited to mental disorders such as, for xample, schizophrenia,
```

dementia or disorders resulting in learning disabilities. In addn., these CGs may be used for the treatment of neurodegenerative conditions such as Alzheimer's disease, Parkinson's disease, conditions resulting from exposure to harmful environmental factors or resulting from a mech. injury. The CGs may also be used to treat an individual suffering from a primary neurodegenerative condition in order to prevent or reduce the appearance of secondary degeneration in addnl. nerves ("nerve rescue"). For example, neural outgrowth of PC12 cells was seen when cells were grown in the presence of nerve growth factor (50 ng/mL) or 1,3-cyclic glycerophosphate (1 .mu.M), but not in the presence of linear .alpha.-glycerophosphate.

cyclic glycerophosphate neuronal differentiation mental disorder; ST antipsychotic schizophrenia cyclic glycerophosphate; Alzheimer disease parkinsonism cyclic glycerophosphate

Anti-Alzheimer's agents Antiparkinsonian agents Antipsychotics Mental disorder Nervous system agents

Schizophrenia

(compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

IT Monoamines

Neurotrophic factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

IT Nerve

(degeneration, prevention of; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

IT Mental disorder

(dementia; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

IT

(differentiation; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

IT Learning

(disorder; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

IT Nerve

(dopaminergic, degeneration of; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

Cell differentiation TT

(inducers; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

ΙT Nerve, disease

(injury, neuronal rescue after; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

Cell differentiation IT

Cell differentiation

(neuronal; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

IT Drug delivery systems

(oral; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

Drug delivery systems IT

```
(osmotic pumps; compns. comprising cyclic glycerophosphates for
        promoting neural differentiation for therapeutic uses)
     Cell proliferation
IT
        (promotion of; compns. comprising cyclic glycerophosphates for
        promoting neural differentiation for therapeutic uses)
     Drug delivery systems
IT
        (topical; compns. comprising cyclic glycerophosphates for promoting
        neural differentiation for therapeutic uses)
IT
     298701-05-0P
     RL: BAC (Biological activity or effector, except adverse); BPN
     (Biosynthetic preparation); BSU (Biological study, unclassified); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     711-07-9P 13507-10-3P 22227-09-4P
IT
     118897-32-8P 123406-35-9P 286020-33-5P
     298701-06-1P 298701-08-3P 298701-09-4P
     298701-78-7P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
      (Preparation); USES (Uses)
        (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     51-61-6, Dopamine, biological studies
                                             59-92-7, biological studies
IT
                       306-08-1, Homovanillic acid
     102-32-9, DOPAC
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
         (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     9001-86-9, Phospholipase C
TΤ
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
      (Uses)
         (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     57-55-6, 1,2-Propanediol, reactions 96-26-4, Dihydroxyacetone
ΙT
     504-63-2, 1,3-Propanediol 770-12-7, Phenyl phosphorodichloridate
                                                               14690-00-7,
     819-83-0, Disodium .beta.-glycerophosphate
                                                 4799-67-1
                                               26776-70-5, Dihydroxyacetone
                                   22002-87-5
     2-Benzyloxy-1,3-propanediol
     dimer
     RL: RCT (Reactant); RACT (Reactant or reagent)
         (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
IT
     187976-16-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP
      (Preparation); RACT (Reactant or reagent)
         (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
IT
      298701-05-0P
      RL: BAC (Biological activity or effector, except adverse); BPN
      (Biosynthetic preparation); BSU (Biological study, unclassified); SPN
      (Synthetic preparation); THU (Therapeutic use); BIOL
      (Biological study); PREP (Preparation); USES (Uses)
         (compns. comprising cyclic glycerophosphates for promoting neural
         differentiation for therapeutic uses)
      298701-05-0 HCAPLUS
RN
      1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide, barium salt (9CI) (CA
 CN
      INDEX NAME)
```

●x Ba

IT 711-07-9P 13507-10-3P 22227-09-4P
 118897-32-8P 123406-35-9P 286020-33-5P
 298701-06-1P 298701-08-3P 298701-09-4P
 298701-78-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)
RN 711-07-9 HCAPLUS
CN 1,3,2-Dioxaphosphorinane, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 13507-10-3 HCAPLUS CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 22227-09-4 HCAPLUS
CN 1,3,2-Dioxaphospholane, 4-methyl-2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 118897-32-8 HCAPLUS

CN 1,3,2-Dioxaphospholane, 2-hydroxy-4-methyl-, 2-oxide, barium salt (9CI) (CA INDEX NAME)

1/2 Ba

RN 123406-35-9 HCAPLUS

CN 9-Octadecenoic acid (92)-, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 286020-33-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 298701-06-1 HCAPLUS

●x Ba

RN 298701-08-3 HCAPLUS

CN 1,3,2-Dioxaphospholane-4-methanol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 298701-09-4 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-one, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 298701-78-7 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-one, 2-hydroxy-, 2-oxide, barium salt (9CI) (CA INDEX NAME)

#### ●1/2 Ba

187976-16-5P IT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(compns. comprising cyclic glycerophosphates for promoting neural

differentiation for therapeutic uses)

RN 187976-16-5 HCAPLUS

1,3,2-Dioxaphosphorinane, 2-hydroxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA CN INDEX NAME)

L24 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2003 ACS

2000:706968 HCAPLUS AN

DN 133:261549 applicante

applicant

```
Cyclic glycerophosphates and analogs for treatment of malignancies
TI
     Shinitzky, Meir
IN
     Yeda Research and Development Co. Ltd., Israel
PA
     PCT Int. Appl., 52 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
     ICM A61K031-00
IC
     1-12 (Pharmacology)
     Section cross-reference(s): 2, 29, 63
FAN.CNT 1
                                                  APPLICATION NO.
                                                                      DATE
                         KIND
                                 DATE
     PATENT NO.
      _____
                                                                      20000324
                                                  WO 2000-IL184
                                 20001005
     WO 2000057864
                           A2
PΙ
                           АЗ
                                 20010531
      WO 2000057864
               AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
               CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
          CU, CZ, DE, DR, DM, DZ, EE, ES, F1, GB, GU, GE, GN, GR, NR, NO, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CL, CM, GA, CN, CM, MI, MD, NF, SN, TD, TG
               CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                                  EP 2000-912876
                                                                     20000324
                               20011219
      EP 1162979
                           A2
               AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                IE, SI, LT, LV, FI, RO
                                                  JP 2000-607615
                                                                      20000324
      JP 2002540145
                           T2
                                 20021126
PRAI IL 1999-129179
                                 19990325
                           Α
                                 20000324
      WO 2000-IL184
      MARPAT 133:261549
os
      Cyclic glycerophosphates as well as some analogs thereof (CGs) are shown
AB
      to increase phosphorylation of intracellular proteins in various cells.
      Such activity is not found with linear .alpha. - or .beta. -
      glycerophosphates. The phosphorylating activity of the CGs render them
      useful in the prevention and treatment of various disorders and diseases
      such as, for example, different kinds of malignancies as well as disorders
      involving hormone and hormone-like signaling. The CGs are also useful for
      promotion of target cell differentiation and for detection of abnormal
      conditions in target cells. For example, CHO cells were incubated with 1
      or 2 .mu.M of 1,3-cyclic propanediol phosphate for 1, 3, 5, and 10 min at
      37.degree.. The level of tyrosine phosphorylated proteins in the cell was
      detd. using monoclonal anti-phosphotyrosine antibodies. Phosphorylation
      was most markedly seen in the band(s) having a mol. wt. of .apprx. 35 and
      45 kilodalton.
      cyclic glycerophosphate protein phosphorylation cell differentiation;
 ST
       antitumor cyclic glycerophosphate protein phosphorylation; antidiabetic
       cyclic glycerophosphate protein phosphorylation; hormone signaling
      phosphorylation cyclic glycerophosphate therapy
 IT
      Antidiabetic agents
      Antitumor agents
       Cytotoxic agents
       Drug delivery systems
          (cyclic glycerophosphates for treatment of malignancies and disorders
          involving hormone-related signaling)
       Hormones, animal, biological studies
 IT
       RL: BSU (Biological study, unclassified); BIOL (Biological study)
           (cyclic glycerophosphates for treatment of malignancies and disorders
          involving hormone-related signaling)
 IT
       Phosphatidylglycerols
```

RL: BSU (Biological study, unclassified); BIOL (Biological study)

62229-50-9, Epidermal growth factor

(cyclic glycerophosphates for tr atment of malignancies and disorders involving hormone-related signaling)

9001-86-9, Phospholipase C IT

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

57-55-6, 1,2-Propanediol, reactions 96-26-4, Dihydroxyacetone 504-63-2, 1,3-Propanediol 770-12-7, Phenyl phosphorodichloridate IT 819-83-0, Disodium .beta.-glycerophosphate 4799-67-1 14690-00-7, 2-Benzyloxy-1,3-propanediol 22002-87-5 26776-70-5, Dihydroxyacetone

RL: RCT (Reactant); RACT (Reactant or reagent) (cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

187976-16-5P IT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

9025-82-5, Phosphodiesterase 9026-43-1, Protein 9013-05-2, Phosphatase IT 106283-10-7, Inositol 1,4,5-trisphosphate kinase 137632-08-7, 142805-58-1, MAPK kinase 139691-76-2, Raf-1 kinase ERK 2 kinase 155215-87-5, JNK kinase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(protein phosphorylating activity of cyclic glycerophosphates useful for treatment of malignancies and disorders involving hormone-related signaling)

TT 298701-05-0P

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

RN 298701-05-0 HCAPLUS

1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide, barium salt (9CI) CN INDEX NAME)

### ●x Ba

711-07-9P 13507-10-3P 22227-09-4P 118897-32-8P 123406-35-9P 286020-33-5P 298701-06-1P 298701-08-3P 298701-09-4P 298701-78-7P

RL: BAC (Biological activity or effector, except adv rse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

RN 711-07-9 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 13507-10-3 HCAPLUS CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 22227-09-4 HCAPLUS CN 1,3,2-Dioxaphospholane, 4-methyl-2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

●1/2 Ba

RN 123406-35-9 HCAPLUS
CN 9-Octadecenoic acid (9Z)-, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 286020-33-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 298701-06-1 HCAPLUS

CN 1,3,2-Dioxaphospholane-4-methanol, 2-hydroxy-, 2-oxide, barium salt (9CI)
 (CA INDEX NAME)

●x Ba

RN 298701-08-3 HCAPLUS

CN 1,3,2-Dioxaphospholane-4-methanol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 298701-09-4 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-one, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

298701-78-7 HCAPLUS

1,3,2-Dioxaphosphorinan-5-one, 2-hydroxy-, 2-oxide, barium salt (9CI) (CA CN INDEX NAME)

#### ●1/2 Ba

IT 187976-16-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(cyclic glycerophosphates for treatment of malignancies and disorders

involving hormone-related signaling)

RN 187976-16-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA INDEX NAME)

L24 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2003 ACS

2000:672262 HCAPLUS AN

DN 134:183352

New biodegradable polymer for drug delivery system poly(D,L-lactide-co-TI ethyl ethylene phosphate)

ΑU Wen, J.; Kim, G. J. A.; Mao, H. Q.; Zhuo, R. X.; Leong, K. W.

Department of Biomedical Engineering, School of Medicine, Johns Hopkins CS University, Baltimore, MD, 21205, USA

SO Proceedings of the International Symposium on Controlled Release of Bioactive Materials (2000), 27th, 664-665 CODEN: PCRMEY; ISSN: 1022-0178

Controlled Release Society, Inc. PB

DT Journal

English LA

63-5 (Pharmaceuticals)

1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 2-ethoxy-1,3,2-dioxaphospholane 2-oxide (9CI) (CA INDEX NAME)

CM 1

CRN 823-31-4

CMF C4 H9 O4 P

RN

326604-67-5 HCAPLUS

CM 2

CRN 95-96-5 CMF C6 H8 O4

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L24 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2003 ACS
AN
     2000:209680 HCAPLUS
DN
     132:256044
     Ocular lens comprising urethane bond-containing polysiloxane macromer
TI
     Watanabe, Tsuyoshi; Baba, Masaki
IN
     Menicon Co., Ltd., Japan
PA
     Eur. Pat. Appl., 38 pp.
     CODEN: EPXXDW
DT
     Patent
LA
     English
IC
     ICM C08F008-44
     ICS C08F008-40; C08F008-34; G02B001-04
     63-7 (Pharmaceuticals)
     Section cross-reference(s): 35, 38
FAN. CNT 1
     PATENT NO.
                      KIND DATE
                                           APPLICATION NO. DATE
                     ----
                                            -----
                            20000329
                                           EP 1999-118558
                                                             19990920
PI
     EP 989138
                      A2
     EP 989138
                      A3
                           20001025
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     US 6346594
                                            US 1999-397674
                                                             19990916
                       Bl
                            20020212
     JP 2000162556
                       A2
                            20000616
                                            JP 1999-263631
                                                             19990917
PRAI JP 1998-266561
                      A
                            19980921
   An ocular lens material comprise a silicone compd. having a zwitterionic
     quaternary ammonium group. The ocular lens material shows excellent
     transparency, oxygen permeability, deposit resistance and wettability to
     tears at the same time. Polysiloxane- polyacrylates were prepd. and
     grafted with sulfopropylammonium betaine to obtain ocular lenses. Phys.
     properties of the lenses were studied.
ST
     ocular lens urethane polysiloxane
     Polyurethanes, biological studies Polyurethanes, biological studies
ΙT
     RL: DEV (Device component use); SPN (Synthetic preparation); THU
```

CMF C3 H7 O4 P

Sackey 09/937386 Page 130

CM

262369-63-1 CRN

(C16 H38 O5 Si4 . C10 H14 O4 . C8 H15 N O2 . C6 H10 O3 . (C2 H6 O CMF Si)n C50 H90 N4 O15 Si2)x

CCI PMS

> 3 、 CM

CRN 262369-61-9

(C2 H6 O Si)n C50 H90 N4 O15 Si2

CCI PMS

PAGE 1-A

PAGE 1-B

CM 4

CRN 17096-07-0 CMF C16 H38 O5 Si4

CM 5

CRN 2867-47-2 CMF C8 H15 N O2

CM 6

CRN 868-77-9 CMF C6 H10 O3

CM 7

CRN 97-90-5 CMF C10 H14 O4

262369-69-7 HCAPLUS RN CN

2-Propenoic acid, 2-methyl-, 1,2-ethanediyl ester, polymer with 2-(dimethylamino)ethyl 2-methyl-2-propenoate, .alpha.-[1,l-dimethyl-9-oxo-11-[1, 3, 3-trimethyl-5-[[[2-[(2-methyl-1-oxo-2propenyl)oxy]ethoxy]carbonyl]amino]cyclohexyl]-5,8-dioxa-10-aza-1silaundec-1-yl]-.omega.-[[1,1-dimethyl-9-oxo-11-[1,3,3-trimethyl-5-[[[2-[(2-methyl-1-oxo-2-propenyl)oxy]ethoxy]carbonyl]amino]cyclohexyl]-5,8dioxa-10-aza-1-silaundec-1-yl]oxy]poly(oxy(dimethylsilylene)], N, N-dimethyl-2-propenamide and 3-[3, 3, 3-trimethyl-1, 1bis[(trimethylsily1)oxy]disiloxanyl]propyl 2-methyl-2-propenoate, compd. with 2-methoxy-1,3,2-dioxaphospholane 2-oxide (9CI) (CA INDEX NAME)

CM 1

CRN 2196-04-5 CMF C3 H7 O4 P

CM 2

262369-62-0 CRN (C16 H38 O5 Si4 . C10 H14 O4 . C8 H15 N O2 . C5 H9 N O . (C2 H6 O CMF Si)n C50 H90 N4 O15 Si2)x CCI **PMS** 

CM 3

CRN 262369-61-9 (C2 H6 O Si)n C50 H90 N4 O15 Si2 CMF CCI

PAGE 1-A

PAGE 1-B

PAGE 1-C

CM 4

CRN 17096-07-0 CMF C16 H38 O5 Si4

CM 5

CRN 2867-47-2 CMF C8 H15 N O2

$$\begin{array}{c|c} & o & \text{CH}_2 \\ \parallel & \parallel \\ \text{Me}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{O}-\text{C}-\text{C}-\text{Me} \end{array}$$

CM 6

CRN 2680-03-7 CMF C5 H9 N O

7 CM

97-90-5 CRN CMF C10 H14 O4

IT 2196-04-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(ocular lens comprising urethane bond-contg. polysiloxane macromer)

2196-04-5 HCAPLUS RN

1,3,2-Dioxaphospholane, 2-methoxy-, 2-oxide (9CI) (CA INDEX NAME) CN

ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2003 ACS L24

2000:133529 HCAPLUS AN

DN 132:175856

Methods using a lysophosphatidic acid receptor agonist for promoting TI survival of myelin-producing cells

Chun, Jerold J. M.; Weiner, Joshua A.; Wickens, Philip L.; Begleiter, IN Leath E.

The Regents of the University of California, USA; Allelix PA Biopharmaceuticals Inc.

PCT Int. Appl., 37 pp. SO CODEN: PIXXD2

Patent DT

LA English

IC

ICM A61K031-665 ICS A61K031-661; C12N005-08; A61P025-28

1-11 (Pharmacology) CC

Section cross-reference(s): 29

FAN.	CNT 1 PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000009139	A2	20000224	WO 1999-US18069	19990810
	WO 2000009139	<b>A3</b>	20000518		

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W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
             MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
             SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                              US 1998-153464
                                                                19980915
                              20001121
     US 6150345
                                              AU 1999-54735
                                                                19990810
                              20000306
     AU 9954735
                        A1
PRAI US 1998-96008P
                        P
                              19980810
                        P
                              19980818
     US 1998-96924P
     US 1998-153464
                        Α
                              19980915
     WO 1999-US18069
                        W
                              19990810
     The invention is in the field of neurobiol., and relates particularly to
AB
     methods useful for enhancing the survival of myelin producing cells, in
     particular Schwann cells and oligodendrocytes, and thereby to treating
     diseases of the nervous system involving loss of myelination or aberrant
     myelination. The methodol. of the invention uses a survival-promoting
     amt. of an lysophosphatidic acid (LPA) receptor agonist, e.g. LPA.
     myelin cell survival lysophosphidate receptor agonist; Schwann cell
ST
     survival lysophosphidate receptor agonist; oligodendrocyte survival
     lysophosphidate receptor agonist; myelination disease lysophosphidate
     receptor agonist; nervous system disease lysophosphidate receptor agonist
     G proteins (guanine nucleotide-binding proteins)
TT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
      (Biological study); PROC (Process)
         (Gi (adenylate cyclase-inhibiting); lysophosphatidic acid receptor
         agonist for promoting survival of myelin-producing cells)
IT
     Receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
      (Biological study); PROC (Process)
         (LPA1/VZG-1/edg-2; lysophosphatidic acid receptor agonist for promoting
         survival of myelin-producing cells)
ΙT
     Nerve, disease
         (demyelination; lysophosphatidic acid receptor agonist for promoting
         survival of myelin-producing cells)
IT
     Animal tissue culture
     Apoptosis
     Myelination
     Nervous system agents
     Oligodendrocyte
     Schwann cell
      Signal transduction, biological
         (lysophosphatidic acid receptor agonist for promoting survival of
         myelin-producing cells)
     Lysophosphatidic acids
IT
      RL: BAC (Biological activity or effector, except adverse); BPR (Biological
      process); BSU (Biological study, unclassified); THU (Therapeutic use);
      BIOL (Biological study); PROC (Process); USES (Uses)
         (lysophosphatidic acid receptor agonist for promoting survival of
         myelin-producing cells)
IT
     Myelin
      RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
      (Biological study); PROC (Process)
         (lysophosphatidic acid receptor agonist for promoting survival of
         myelin-producing cells)
 IΤ
      Gene, animal
      RL: BPR (Biological process); BSU (Biological study, unclassifi d); BIOL
```

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(Biological study); PROC (Process)
        (lysophosphatidic acid receptor; lysophosphatidic acid receptor agonist
        for promoting survival of myelin-producing cells)
IT
     Receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (lysophosphatidic acid; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
IT
     Heregulins
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (neuregulin .beta.; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
     Phosphorylation, biological
IT
        (protein; lysophosphatidic acid receptor agonist for promoting survival
        of myelin-producing cells)
IT
     Lysophosphatidic acids
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (receptors; lysophosphatidic acid receptor agonist for promoting
        survival of myelin-producing cells)
TT
     Receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (sphingosine 1-phosphate; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
     Multiple sclerosis
IT
        (therapeutic agents; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
     26993-30-6, Sphingosine 1-phosphate
IT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
                                 259225-84-8P
     169736-88-3P 259225-83-7P
                                               259225-85-9P
TΤ
     259225-86-0P
                    259225-87-1P
                                  259231-37-3P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
     65528-98-5
TΤ
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
     115926-52-8, Phosphoinositide 3-kinase
                                              149147-12-6, Akt kinase
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
                 18704-66-0P
                                83258-36-0P 259231-36-2P
     111-58-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
                                                         112-77-6, Oleoyl
                          112-16-3, Lauroyl chloride
IT
     87-66-1, Pyrogallol
                                                                      6286-43-7,
                                     156-87-6, 1-Propanol-3-amine
                141-43-5, reactions
     chloride
```

7719-09-7, Thionyl chloride 7790-94-5, 1,2,3-Cyclohexanetriol Chlorosulfuric acid 10025-87-3, Phosphorus oxychloride 25496-72-4, Monoolein 26402-26-6, Monocaprylin RL: RCT (Reactant); RACT (Reactant or reagent) (reaction; lysophosphatidic acid receptor agonist for promoting

survival of myelin-producing cells)

IT 169736-88-3P 259225-83-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(lysophosphatidic acid receptor agonist for promoting survival of myelin-producing cells)

RN 169736-88-3 HCAPLUS

CN

9-Octadecenoic acid (92)-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

Na

RN 259225-83-7 HCAPLUS

Octanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, CN sodium salt (9CI) (CA INDEX NAME)

Na

L24 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2003 ACS

1999:576934 HCAPLUS AN

DN 131:185194

TI Preparation of cyclic nucleotides as FBPase inhibitor prodrugs

IN Erion, Mark D.; Reddy, K. Raja; Robinson, Edward D.

Metabasis Therapeutics, Inc., USA

SO PCT Int. Appl., 240 pp.

CODEN: PIXXD2

DT Patent

LA English

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ICM C07H019-00
     33-9 (Carbohydrates)
     Section cross-reference(s): 7, 63
FAN.CNT 2
                                               APPLICATION NO.
                                                                  DATE
                        KIND DATE
     PATENT NO.
                        ____
                                               WO 1999-US4908
                                                                  19990305
                         A2
                               19990910
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     WO 9945016
     WO 9945016
                         A3
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              DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
              MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
              TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
              ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
              CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                               CA 1999-2322487
                               19990910
                                                                  19990305
     CA 2322487
                         AA
                                               AU 1999-30699
                                                                  19990305
                         A1
                               19990920
     AU 9930699
                                               EP 1999-912300
                                                                  19990305
                               20001220
     EP 1060182
                         A2
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
                                               JP 2000-534558
                                                                  19990305
                         T2
                               20020219
     JP 2002505333
PRAI US 1998-77164P
                         P
                               19980306
     US 1998-77165P
                         ₽
                               19980306
     WO 1999-US4908
                         W
                               19990305
OS
     MARPAT 131:185194
GI
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Prodrugs of phosphorus-contg. nucleotides I, wherein V is selected from the group consisting of H, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R9; or together V and Z are connected via 3-5 atoms to form a cyclic group, optionally contg. 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or together V and Z are connected via 3-5 atoms to form a cyclic group, optionally contg. 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the oxygen attached to the phosphorus. Together V and W are connected via 3 carbon atoms to form an optionally substituted cyclic group contg. 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; W and R are independently selected from the group consisting of H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R9. Z is selected from the group consisting of -CHR2OH, -CHR2OC(0)R3, -CHR2OC(S)R3, -CHR2OC(S)OR3, -CHR2OC(0)SR3, -CHR2OCO2R3,

```
-OR2, -SR2, -CHR2N3, -CH2aryl, -CH(aryl)OH, -CH(CH=CR22)OH,
    -CH(C.tplbond.CR2)OH, -R2, -NR22, -OCOR3, -OCO2R3, -SCOR3, -SCO2R3,
     -NHCOR2, -NHCO2R3, -CH2NHaryl, (CH2)p-OR2, and (CH2)p-SR2; -R2 is an R3 or
     -H; R3 is selected from the group consisting of alkyl, aryl, aralkyl, and
    alicyclic; and R9 is selected from the group consisting of alkyl, aralkyl,
    and alicyclic; p is an integer from 2 to 3. With the proviso that (a) V,
     Z, W, and R are not all -H; and (b) when Z is -R2, then at least one of V
     and W is not -H, or -R9; and M is selected from the group that attached to
     PO32-, P2063-, or P3094- is biol. active in vivo, and that is attached to
     the phosphorus in I via a carbon, oxygen, or nitrogen atom; and
     pharmaceutically acceptable prodrugs and salts thereof. Thus, cyclic
     nucleotide I (M = adenine-9-.beta.-D-arabinofuranos-5'-yl; V = 4-pyridyl;
     Z = W = R = H) was prepd. and tested as prodrug human liver FBPase
     inhibitor (EC50 < 10 .mu.M).
     drug delivery system nucleotide prepn enzyme inhibitor; cyclic nucleotide
ST
     prepn enzyme FBPase inhibitor prodrug
     Drug delivery systems
TΤ
        (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
IT
     Nucleotides, preparation
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); IMF (Industrial manufacture); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
     Drug delivery systems
IT
        (prodrugs; prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
IT
     180255-38-3
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (human liver; prepn. of cyclic nucleotides as FBPase inhibitor
        prodrugs)
                                                               213198-79-9P
                                                213198-14-2P
                                 213125-14-5P
IT
     59354-01-7P
                   85665-04-9P
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                                                  213201-50-4P
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     213201-52-6P
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                                   240434-27-9P
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                    240434-26-8P
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     240434-55-3P 240434-56-4P 240434-57-5P
     240434-58-6P 240434-59-7P 240434-60-0P
     240487-26-7P 240487-27-8P 240487-28-9P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); IMF (Industrial manufacture); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
         (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
                                                   9001-78-9
     9001-40-5, Glucose-6-phosphate dehydrogenase
IT
     Carboxyesterase
     RL: CAT (Catalyst use); USES (Uses)
         (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
                                                               110-70-3,
                                 110-60-1, 1,4-Butanediamine
     78-77-3, Isobutyl bromide
IT
                                                                   814-49-3,
                                      498-60-2, 3-Furfuraldehyde
     N, N'-Dimethylethylene diamine
                                                                   2627-69-2
     Diethylchlorophosphate 1826-67-1, Vinylmagnesium bromide
     2859-68-9, 2-Pyridine propanol 4704-94-3
                                                  4799-68-2
                                                             5413-85-4,
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5-Amino-4,6-dichloropyrimidin
                                     5813-64-9, Neopentylamine
                                                                  14215-97-5
                  50409-12-6 65641-62-5 106941-25-7 213124-94-8
     41368-63-2
     213248-53-4
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
     19790-60-4P
                   23274-21-7P
                                 33235-31-3P
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     240434-43-9P
                    240434-48-4P
                                   240434-61-1P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
IT
     240434-53-1P 240434-54-2P 240434-55-3P
     240434-56-4P 240434-57-5P 240434-58-6P
     240434-59-7P 240434-60-0P 240487-27-8P
     240487-28-9P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); IMF (Industrial manufacture); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
RN
     240434-53-1 HCAPLUS
     9H-Purin-6-amine, 9-[5-0-(2-oxido-4-phenyl-1,3,2-dioxaphosphorinan-2-yl)-
CN
     .beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)
```

### Absolute stereochemistry.

RN 240434-54-2 HCAPLUS

CN 9H-Purin-6-amine, 9-[5-O-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

### Absolute stereochemistry.

RN 240434-55-3 HCAPLUS

CN 6H-Purin-6-one, 1,9-dihydro-9-[(2R,5S)-tetrahydro-5-[[[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy]methyl]-2-furanyl]- (9CI) (CF INDEX NAME)

Absolute stereochemistry.

RN 240434-56-4 HCAPLUS

CN 1H-1,2,4-Triazole-3-carboxamide, 1-[5-0-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]-.beta.-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240434-57-5 HCAPLUS

CN 9H-Purin-6-amine, 2-fluoro-9-[5-0-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240434-58-6 HCAPLUS

CN 9H-Purin-6-amine, 9-[(2R,5S)-tetrahydro-5-[[[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240434-59-7 HCAPLUS
CN Uridine, 2'-deoxy-5-fluoro-5'-O-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240434-60-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-[[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy]ethoxy]methyl]- (9CI) (CA INDEX NAME)

RN 240487-27-8 HCAPLUS

CN 9H-Purin-6-amine, 9-[5-0-[5-[(acetyloxy)methyl]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

240487-28-9 HCAPLUS RN

Uridine, 2'-deoxy-5-fluoro-3',5'-bis-O-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]- (9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2003 ACS L24

1998:169488 HCAPLUS AN

128:257656 DN

Preparation of amphiphilic glycerols or ethyleneglycols as TI phosphatidylcholine synthesis inhibitors and antitumors

IN

Attard, George Simon; McGuigan, Christopher; Riley, Patrick Anthony University of Southampton, UK; Attard, George Simon; McGuigan, PA

Christopher; Riley, Patrick Anthony

PCT Int. Appl., 57 pp. SO

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61L031-00

33-6 (Carbohydrates) CC

Section cross-reference(s): 1

FAN.CNT 1

APPLICATION NO. DATE PATENT NO. KIND

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PI · WO 9809668
                        A2
                             19980312
                                             WO 1997-GB2410
                                                               19970908
     WO 9809668
                        A3
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             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
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             GN, ML, MR, NE, SN, TD, TG
     AU 9741285
                        A1
                             19980326
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PRAI GB 1996-18634
                             19960906
     WO 1997-GB2410
                             19970908
OS
     MARPAT 128:257656
AB
     Use of an amphiphilic compd. in the manuf. of a medicament for the
     inhibition of phosphatidylcholine synthesis, said amphiphilic compd. have
     the following properties: (i) the compd. comprises a non-ionic, cationic
     or anionic hydrophilic head group and a hydrophobic tail group; (ii) the
     head group has a cross section A and the tail group has a cross section B
     such that the ratio B:A is less than 0.7:1; (iii) the tail group comprises
     a straight hydrocarbon chain having from 8 to 18 carbon atoms; and i.v.
     the amphiphilic compd. has a membrane/water partition coeff. of more than
     1 x 10-3. Thus, 1-0-(5', 5'-dimethyl-1', 3'-dioxa-2'-phosphacyclohexane-2'-
     oxide)-2-0-methyl-3-0-hexadecyl-rac-glycerol was prepd. and tested for its
     antitumor and hemolytic activity (HC50 = 0.044-0.178).
ST
     hemolytic activity phosphatidylcholine inhibitor antitumor; ethyleneglycol
     amphiphilic prepn phosphatidylcholine inhibitor antitumor; amphiphilic
     glycerol prepn phosphatidylcholine inhibitor antitumor
IT
     Antitumor agents
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
IT
     Phosphatidylcholines, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
IT
     Amphiphiles
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
IT
     Glycols, preparation
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
TT
     57-09-0P
               1119-97-7P
                              3055-98-9P
                                           5698-39-5P
                                                         13149-87-6P
     15590-96-2P
                   24233-81-6P
                                  27847-86-5P
                                                 29908-17-6P 194147-98-3P
     204924-40-3P 204924-42-5P 204924-43-6P
     204924-44-7P
                    204924-45-8P
                                    204924-47-0P 204924-48-1P
                                 204924-53-8P
     204924-50-5P 204924-52-7P
                                                  204924-56-1P
     204924-58-3P
                     204924-59-4P
                                    204924-60-7P
                                                    204924-61-8P
                                                                    204924-62-9P
     204924-79-8P
                    205132-42-9P, Mitelfosine
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
     100-79-8, Solketal
                           143-15-7, 1-Bromododecane 626-67-5, N-Methyl
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Sackey 09/937386 Page 146
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piperidine RL: RCT (Reactant); RACT (Reactant or r agent) (prepn. of amphiphilic glycerols or ethyleneglycols as phosphatidylcholines synthesis inhibitors and antitumors) TT 112-82-3P, 1-Bromohexadecane 140-72-7P 6145-69-3P 7252-87-1P 36324-72-8P 71221-96-0P 10395-09-2P 14847-87-1P 41672-91-7P 84337-41-7P 162758-12-5P 162870-36-2P 194147-97-2P 82002-20-8P 204924-77-6P 204924-74-3P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of amphiphilic glycerols or ethyleneglycols as phosphatidylcholines synthesis inhibitors and antitumors) 194147-98-3P 204924-40-3P 204924-42-5P IT 204924-43-6P 204924-48-1P 204924-52-7P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of amphiphilic glycerols or ethyleneglycols as phosphatidylcholines synthesis inhibitors and antitumors) 194147-98-3 HCAPLUS RN CN 1,3,2-Dioxaphosphorinane, 5-dodecyl-2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 204924-40-3 HCAPLUS
CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-tetradecyl-, 2-oxide (9CI) (CA INDEX NAME)

RN 204924-42-5 HCAPLUS CN 1,3,2-Dioxaphosphorinane, 5-hexadecyl-2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 204924-43-6 HCAPLUS

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-octadecyl-, 2-oxide (9CI) (CA INDEX NAME)

RN 204924-48-1 HCAPLUS CN 1,3,2-Dioxaphosphorinane, 2-[3-(hexadecyloxy)-2-methoxypropoxy]-, 2-oxide (9CI) (CA INDEX NAME)

RN 204924-52-7 HCAPLUS
CN 1,3,2-Dioxaphosphorinane, 2-[3-(hexadecyloxy)-2-methoxypropoxy]-5,5dimethyl-, 2-oxide (9CI) (CA INDEX NAME)

L24 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1997:237764 HCAPLUS

DN 126:220705

TI Tumor metastasis inhibitors containing 1-0-acylglycerol-2,3-phosphates

IN Kobayashi, Susumu; Matsumoto, Myoko; Onimura, Kenjiro; Aketo, Hitoshi; Aragai, Kyoko; Mukai, Michiko

PA Sagami Chem Res, Japan

SO Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM A61K031-665

ICS C07F009-10; C07F009-6574

CC 1-6 (Pharmacology)

Section cross-reference(s): 33

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE
PI JP 09025235 A2 19970128 JP 1995-177170 19950713
PRAI JP 1995-177170 19950713

```
Sackey 09/937386 Page 148
    MARPAT 126:220705
OS
GI
   o-cor
                 Ι
     The metastasis inhibitors contain the title compds. I (R = C2-30 linear or
AB
     branched alkyl, alkenyl, alkynyl which may contain cycloalkane ring; M =
     H, counter cation) as active ingredients. I (COR = palmitoyl, M = Na)
     (prepn. given) at 25 .mu.M showed >99% inhibition against
     1-O-oleoyllysophosphatidic acid-induced infiltration of rat ascites
     hepatoma cell (MM1) into a cultured monolayer of peritoneal mesothelial
     cells, vs. 96% at 12.5 .mu.M for PHYLPA.
     acylglycerol phosphate prepn metastasis inhibitor; tumor metastasis
     inhibitor acylglycerol phosphate; glycerophospholipid prepn tumor
     metastasis inhibitor
IT
     Antitumor agents
        (metastasis; prepn. of 1-O-acylglycerol-2,3-phosphates as tumor
        metastasis inhibitors)
     168217-09-2P 168217-10-5P 169736-88-3P
IT
     188171-56-4P 188171-60-0P 188171-62-2P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
         (prepn. of 1-0-acylglycerol-2,3-phosphates as tumor metastasis
        inhibitors)
                                        112-80-1, 9-Octadecenoic acid (Z)-,
     57-10-3, Palmitic acid, reactions
ΙT
                                                        10030-73-6 14347-83-2
                            506-30-9, Eicosanoic acid
     reactions 373-49-9
     89155-39-5, 9-Hexadecynoic acid
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of 1-O-acylglycerol-2,3-phosphates as tumor metastasis
        inhibitors)
                                  129784-87-8P
                                                 150447-02-2P
                                                                 188171-53-1P
     14347-78-5P
                   125226-51-9P
ΤT
                    188171-55-3P
                                                  188171-58-6P
                                                                  188171-59-7P
                                  188171-57-5P
     188171-54-2P
                                   188182-88-9P
                    188182-87-8P
     188171-61-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
         (prepn. of 1-0-acylglycerol-2,3-phosphates as tumor metastasis
        inhibitors)
     168217-09-2P 168217-10-5P 169736-88-3P
     188171-56-4P 188171-60-0P 188171-62-2P
```

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

(prepn. of 1-O-acylglycerol-2,3-phosphates as tumor metastasis

9-H xadec noic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

inhibitors)
168217-09-2 HCAPLUS

RN

yl]methyl ester, sodium salt, (9Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

Na

RN 168217-10-5 HCAPLUS

CN 9-Hexadecynoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 169736-88-3 HCAPLUS

CN 9-Octadecenoic acid (92)-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

Na

RN 188171-56-4 HCAPLUS

9-Hexadecenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (9E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

Na

188171-60-0 HCAPLUS RN

Nonanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, CN sodium salt, (R) - (9CI) (CA INDEX NAME)

#### Absolute stereochemistry.

Na

RN 188171-62-2 HCAPLUS

Eicosanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

#### Absolute stereochemistry.

Na

L24 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2003 ACS

1997:224038 HCAPLUS AN

DN 126:212447

TI Phosphorous-containing dipeptide inhibitors of cysteine and serine

IN Mallamo, John P.; Bihovsky, Ron; Tao, Ming; Wells, Gregory J.

PA

Cephalon, Inc., USA PCT Int. Appl., 59 pp. SO

CODEN: PIXXD2

DT Patent

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

```
LA
     English
     ICM A61K031-66
IC
         A61K031-665; A61K031-675; C07F009-09; C07F009-32; C07F009-40;
     ICS
           C07F009-53; C07F009-572; C07F009-6533; C07F009-6574
CC
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1, 7
FAN.CNT 1
     PATENT NO.
                                              APPLICATION NO.
                       KIND DATE
                                                                 DATE
     WO 9703679
PI
                        Al
                              19970206
                                              WO 1996-US11625 19960712
         W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
              ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,
              LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
              SE, SG
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN
     US 5639732
                              19970617
                                              US 1996-679342
                        A
                                                                 19960710
     CA 2226414
                        AA
                              19970206
                                              CA 1996-2226414
                                                                19960712
     AU 9664583
                        A1
                              19970218
                                              AU 1996-64583
                                                                 19960712
     EP 871454
                                              EP 1996-923756
                        A1
                              19981021
                                                                 19960712
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
         R:
              IE, FI
     JP 11509231
                         T2
                              19990817
                                              JP 1996-506762
                                                                 19960712
PRAI US 1995-1491P
                        P
                              19950717
     US 1996-679342
                        Α
                              19960710
     WO 1996-US11625
                        W
                              19960712
OS
     MARPAT 126:212447
GI
```

$$\begin{array}{c|c}
0 & \text{II} & \text{(O)} \, \text{mR}^4 \\
-\text{(O)} \, z & \text{P} & \text{(O)} \, \text{nR}^5 & \text{I}
\end{array}$$

The present invention is directed to novel phosphorous-contg. inhibitors of cysteine or serine proteases of the formula X-W-Y-CH(R2)-CO-NH-CH(R1)-CO-[CH(R3)]t-Q wherein: X = e.g., C6-C14 aryl, heteroaryl with C6-C14 ring atoms, C1-C10 alkyl (un) substituted with one or more J groups, C1-C10 alkoxy; W = CO, SO2; Y = NH, (CH2)k where k = 0-3; R1 and R2 are independently, e.g., H, C1-C14 alkyl (un) substituted with one or more J groups, C3-C10 cycloalkyl (un) substituted with one or more J groups, C3-C10 cycloalkyl (un) substituted with one or more J groups; R3 = e.g., H, lower alkyl, aryl, heteroaryl; t = 0 or 1; Q = I wherein m, n, and z are independently 0 or 1; R4 and R5 are independently, e.g., H, lower alkyl (un) substituted with J, heteroaryl (un) substituted with J, or taken together to form a 5-8 membered heterocyclic ring (un) substituted with J; J = e.g., halogen, alkyl, guanidino, alkoxy. Thus, e.g., substitution reaction of Z-Leu-Phe-CH2Br with

II

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bis(phenethyl)phosphate afforded dipeptide deriv. II (Z = PhCH2O2C) in 62%
     yield which exhibited 99% inhibition of calpain I at 0.1 .mu.M. Methods
     for the use of the proteas inhibitors are also described.
ST
     dipeptide prepn inhibitor cysteine serine protease; peptide phosphonate
     cysteine serine protease inhibitor; phosphorous contg peptide serine
     protease inhibitor; cysteine protease inhibitor phosphorous contg peptide
IT
     Dipeptides
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (phosphono analogs; prepn. of phosphorous-contg. dipeptide inhibitors
        of cysteine and serine protease)
IT
     78990-62-2, Calpain
     RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
     (Miscellaneous); BIOL (Biological study); PROC (Process)
        (I; prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and
        serine protease)
TT
     187976-26-7P
                    187976-27-8P
                                   187976-28-9P
                                                   187976-29-0P
                                                                  187976-31-4P
                                   187976-34-7P
     187976-32-5P
                    187976-33-6P
                                                   187976-35-8P
                                                                  187976-36-9P
     187976-37-0P
                    187976-38-1P
                                   187976-39-2P
                                                   187976-40-5P
                                                                  187976-41-6P
     187976-42-7P
                    187976-43-8P
                                   187976-44-9P
                                                   187976-45-0P
                                                                  187976-46-1P
     187976-47-2P
                    187976-48-3P
                                   187976-49-4P
                                                   187976-50-7P
                                                                  187976-51-8P
     187976-52-9P
                    187976-53-0P
                                   187976-54-1P
                                                   187976-55-2P
                                                                  187976-56-3P
     187976-57-4P
                    187976-58-5P
                                   187976-59-6P 188010-56-2P
     188013-51-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses) (prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and
        serine protease)
ΙT
     37259-58-8, Serine protease
                                   37353-41-6, Cysteine protease
     RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
     (Miscellaneous); BIOL (Biological study); PROC (Process)
        (prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and
        serine protease)
     60-12-8, Phenethyl alcohol 103-63-9, (2-Bromoethyl)benzene
Dibutyl phosphate 109-70-6, 1-Bromo-3-chloropropane 110-9
                                                                     107-66-4,
                                                             110-91-8,
     Morpholine, reactions 298-07-7, Bis(2-ethylhexyl) phosphate
                                                                      644-97-3,
     Phenyl dichlorophosphine 677-24-7, Methyl dichlorophosphate
                                                                      813-78-5,
     Dimethyl phosphate
                        868-85-9, Dimethyl phosphite 993-13-5,
                                                                 1623-08-1,
     Methylphosphonic acid 1571-33-1, Phenylphosphonic acid
     Dibenzyl phosphate 1809-19-4, Dibutyl phosphite 2018-66-8,
     N-Benzyloxycarbonyl-leucine 3283-12-3, Dimethylphosphinic acid
     3445-11-2, 1-(2-Hydroxyethyl)-2-pyrrolidinone
                                                     3647-69-6,
     N-(2-Chloroethyl)morpholine hydrochloride
                                                 4552-91-4
                                                             13826-35-2
     14690-00-7, 2-Benzyloxy-1,3-propanediol 15948-60-4, Bis (4-
     chlorophenyl)phosphine oxide
                                    20434-05-3
                                                 58521-45-2.
     N-tert-Butoxycarbonyl-leucinal
                                      95322-86-4
                                                    110972-27-5,
     N, N-Diisopropylmethylphosphonamidic chloride
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and
        serine protease)
IT
                 2511-09-3P, Ethyl phenylphosphinate
     2227-43-2P
                                                        7357-67-7P
     13317-44-7P, Ethyl phenylphosphinic acid 14561-21-8P,
     Bis(2-phenylethyl)phosphinic acid
                                        18593-19-6P
                                                       19236-48-7P
                                20148-17-8P
                                              24935-94-2P, Dipentylphosphinic
                   19236-61-4P
     19236-58-9P
            31735-80-5P 39063-70-2P 50972-25-3P
     acid
                                                      97785-51-8P
     101523-04-0P 118252-76-9P 118930-87-3P 151091-71-3P 187975-99-1P
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187976-12-1P 187976-03-0P 187976-05-2P 187976-07-4P 187976-01-8P 187976-20-1P 187976-18-7P 187976-14-3P 187976-16-5P 187976-25-6P 187976-60-9P 187976-23-4P 187976-24-5P 187976-22-3P 187976-61-0P 187976-62-1P 187976-63-2P 187976-64-3P 187976-68-7P 187976-69-8P 187976-66-5P 187976-67-6P 187976-65-4P 187976-71-2P 187976-72-3P 187976-73-4P 187976-74-5P 187976-70-1P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and serine protease)

IT 57616-74-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and serine protease)

IT 188010-56-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and serine protease)

RN 188010-56-2 HCAPLUS

CN Carbamic acid, [3-methyl-1-[[[3-[[2-oxido-5-(phenylmethoxy)-1,3,2-dioxaphosphorinan-2-yl]oxy]-2-oxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester, [2[S(S)]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

#### IT 187976-16-5P 187976-62-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and serine protease)

RN 187976-16-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA INDEX NAME)

RN 187976-62-1 HCAPLUS

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Sackey 09/937386 Page 154
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I, 3, 2-Dioxaphosphorinane, 2-methoxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA INDEX NAME)

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Ph-CH<sub>2</sub>-O
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L24 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2003 ACS
    1996:672866 HCAPLUS
AN
DN
     125:339157
    Preparation of lysophosphatidic acids for treating hyperproliferative
TI
    conditions
    Piazza, Gary A.; Mazur, Adam W.
IN
    The Procter & Gamble Company, USA
PA
    U.S., US14 pp., Cont. of U.S. Ser. No. 980,814, abandoned.
SO
     CODEN: USXXAM
     Patent
DT
LA
     English
     ICM A61K031-66
IC
NCL
     514110000
     63-8 (Pharmaceuticals)
     Section cross-reference(s): 28, 62
FAN.CNT 1
                     KIND DATE
                                          APPLICATION NO. DATE
     PATENT NO.
                                           _____
     _____
                           -----
                            19961015
                                          US 1994-334888 19941104
     US 5565439
PΙ
                     A
PRAI US 1992-980814
                            19921124
     MARPAT 125:339157
     The invention involves a method for treating hyperproliferative conditions
AB
     (no data ) in mammalian epithelial cells, comprising administering a
     lysophosphatidic acid deriv. (prepn. given) RC(:X)XCH2CH2CH2YPO3H2 or its
     cyclic deriv. [Y = 0 or CH2; Z = H, XH or halo; X = 0 or S; R =
     (un) substituted (un) satd., straight or branched Cll-23 alkyl].
     1-Oleoylglycerol-3-phosphate is an example. The compns. are usable for
     the treatment of skin cancer, psoriasis, dandruff, etc.
     lysophosphatidic acid prepn skin hyperproliferative conditions
ST
     Skin, disease
IT
        (lysophosphatidic acids for treating skin hyperproliferative
        conditions)
     Lysophosphatidic acids
TT
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. as agent for treating skin hyperproliferative conditions)
     1660-95-3P, Tetraisopropyl methylenediphosphonate 5736-03-8P
IT
                   146491-08-9P 146491-10-3P 146508-57-8P
     146491-07-8P
     158271-50-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (intermediate in prepn. of lysophosphatidic acid deriv. for treating
        skin hyperproliferative conditions)
     146565-97-1P
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP
     (Preparation); RACT (Reactant or reagent)
        (prepn. as agent for treating skin hyperproliferative conditions)
```

146491-11-4P 158271-52-4P 168217-08-1P IT 65528-98-5P RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. as agent for treating skin hyperproliferative conditions) 1623-08-1, Dibenzyl phosphate 4161-56-2, 3-Bromo-2-fluoro-1-propanol TΤ 24909-72-6, Oleic anhydride 32899-41-5 50651-75-7, Silver 22323-82-6 60134-06-7 Dibenzyl phosphate RL: RCT (Reactant); RACT (Reactant or reagent) (reactant in prepn. of lysophosphatidic acid deriv. for treating skin hyperproliferative conditions) IT 146565-97-1P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. as agent for treating skin hyperproliferative conditions) 146565-97-1 HCAPLUS RN Hexadecanoic acid, {(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-CN yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 168217-08-1P

RN 168217-08-1 HCAPLUS
CN Hexadecanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

L24 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1995:1006821 HCAPLUS

DN 124:76506

- TI Preparation of 1-O-acylglycerol-2,3-phosphates and DNA polymerase .alpha. inhibitors containing them
- IN Kobayashi, Susumu; Imai, Nobuyuki; Onimura, Kenjiro; Shinagawa, Rumi; Nakamura, Shuko; Murofushi, Kimiko

PA Sagami Chem Res, Japan

SO Jpn. Kokai Tokkyo Koho, 6 pp.

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Sackey 09/937386 Page 156
     CODEN: JKXXAF
DT
     Patent
LA
     Japanes
IC
     ICM C07F009-09
     ICS A61K031-665
     1-6 (Pharmacology)
     Section cross-reference(s): 7
FAN. CNT 1
     JP 022522
     PATENT NO.
                                              APPLICATION NO.
                                                                 DATE
                              _____
                                               ------
     JP 07258278
                         A2
                              19951009
PI
                                               JP 1994-72837
                                                                 19940318
PRAI JP 1994-72837
                              19940318
     MARPAT 124:76506
OS
GI
CH2OCOR1
Ċн — о (
CH2-0
          OM
AB
     The title compds. I (R1 = C10-30 linear or branched alkenyl, alkynyl; M =
     H, counter cation) and DNA polymerase .alpha. inhibitors contg. I as
     active ingredients are claimed. The inhibitors are useful as antitumor
     agents. Activities of DNA polymerase .alpha. to produce DNA from deoxyribonucleotide triphosphate were 82 and 11% in the presence of I
     [COR1 = (Z)-hexadecenoyl, M = Na] (prepn. given) at 5 or 40 .mu.g/mL,
     resp.
ST
     DNA polymerase inhibitor acylglycerol phosphate; neoplasm inhibitor
     acylglycerol phosphate
IT
     Neoplasm inhibitors
        (DNA polymerase .alpha. inhibitors contg. 1-O-acylglycerol-2,3-
        phosphates as antitumor agents)
IT
     172360-60-0P 172489-74-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (DNA polymerase .alpha. inhibitors contg. 1-0-acylglycerol-2,3-
        phosphates as antitumor agents)
IT
     373-49-9, (2)-9-Hexadecenoic acid
                                            89155-39-5, 9-Hexadecynoic acid
     RL: RCT (Reactant); RACT (Reactant or reagent)
(O-acylation of isopropylideneglycerol; DNA polymerase .alpha.
        inhibitors contg. 1-0-acylglycerol-2,3-phosphates as antitumor agents)
IT
     100-79-8, 2,3-0-Isopropylideneglycerol
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (O-acylation of; DNA polymerase .alpha. inhibitors contg.
     1-O-acylglycerol-2,3-phosphates as antitumor agents) 37515-61-0P 172360-57-5P 172360-58-6P 172360-59-7P
IT
```

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(reaction with POCl.beta.; DNA polymerase .alpha. inhibitors contg.

(deprotection of; DNA polymerase .alpha. inhibitors contg. 1-0-acylglycerol-2,3-phosphates as antitumor agents)

RL: RCT (Reactant); RACT (Reactant or reagent)

(Reactant or reagent)

288-88-0, 1H-1,2,4-Triazole

IT

1-O-acylglycerol-2, 3-phosphates as antitumor agents)

IT 10025-87-3, Phosphoryl chloride

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction with triazole; DNA polymerase .alpha. inhibitors contg.

1-O-acylglycerol-2, 3-phosphates as antitumor agents)

IT 9012-90-2, DNA polymerase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(.alpha.; DNA polymerase .alpha. inhibitors contg. 1-O-acylglycerol-2,3-phosphates as antitumor agents)

IT 172360-60-0P 172489-74-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(DNA polymerase .alpha. inhibitors contg. 1-O-acyiqlycerol-2,3-

phosphates as antitumor agents)

RN 172360-60-0 HCAPLUS

CN 9-Hexadecynoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

Na

RN 172489-74-6 HCAPLUS

CN

9-Hexadecenoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

● Na

L24 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1995:638236 HCAPLUS

DN 123:144502

TI Method for preparation of 1-0-acylglycerol 2,3-cyclic phosphate

IN Kobayashi, Susumu; Imai, Nobuyuki; Shinagawa, Rumi; Takahashi, Hideyori

PA Sagami Chem Res, Japan

SO Jpn. Kokai Tokkyo Koho, 31 pp.

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

```
CODEN: JKXXAF
DT
     Patent
LA
     Japanese
    ICM C07F009-09
IC
     ICS C07F009-6574
    A61K031-665; A61K037-22
     33-6 (Carbohydrates)
     Section cross-reference(s): 1, 7
FAN.CNT 1
     PATENT NO.
                      KIND
                            DATE
                                           APPLICATION NO.
                                                            DATE
                                           -----
                            19940816
PI
     JP 06228169
                      A2
                                           JP 1993-40657
                                                            19930205
PRAI JP 1993-40657
                            19930205
    CASREACT 123:144502; MARPAT 123:144502
GI
```

The title compd. [I; R = linear or branched C1-30 alkyl or C2-30 alkenyl optionally contg. a cycloalkane or an arom. ring; M = H, alkali or alk. earth metal, (un)substituted ammonium] is prepd. by reacting 1-O-acylglycerol RCO2CH2CH(OH)CH2OH (R = same as above) with a phosphorylating agent X1X2X3P(O) [X1 = halo, imidazolyl, triazolyl; X2 = halo, imidazolyl, triazolyl, (un)substituted PhO or alkoxy; X3 = imidazolyl, triazolyl, (un)substituted PhO or alkoxy, substituted amino] followed by hydrolysis. An optically active intermediate (II; m, n = O-15 integer; R1, R2 = H, HO-protective group) is also prepd. This process gives, in particular, lysophosphatidic acid PHYLPA I (R = Q, M = Na) which is a potent DNA polymerase .alpha. inhibitor and potentially useful as an antitumor agent (no data). Thus, 1-O-{(9S,10R)-9,10-methanohexadecanoyl}-sn-glycerol (prepn. given) in THF was added to a soln. of phosphoryl tristriazolide in THF which was prepd. by reacting triazole with POC13 and Et3N in THF, and the resulting mixt. was stirred at room temp. for 20 min, added to 2% aq. HCl, and extd. with Et2O. The ether ext. was dried over

```
anhyd. Na2SO4, treated with NaH in Et2O, and extd. with distd. water
     followed by freeze-drying the water ext. to give 97% optically active
     title compd. (III).
ST
     acylglycerol cyclic phosphate prepn antitumor; DNA polymerase alpha
     inhibitor PHYLPA
ΙT
     Neoplasm inhibitors
        (prepn. of O-acylglycerol cyclic phosphate as DNA polymerase inhibitors
        and antitumor agents)
IT
     14347-78-5P, 2,3-0-Isopropylidene-sn-glycerol
                                                      18172-01-5P,
                                     151707-28-7P
                                                     151707-29-8P
     3-Oxabicyclo[3.1.0]hexan-2-ol
                                                                    151707-30-1P
     151707-31-2P
                    151766-40-4P
                                   151766-41-5P
                                                                  151766-43-7P
                                                   151766-42-6P
                    151766-45-9P
                                   151766-46-0P
                                                   151766-48-2P
     151766-44-8P
                                                                  151766-49-3P
                    164215-55-8P
                                   164215-57-OP
     151766-50-6P
                                                   164323-39-1P
                                                                  164323-40-4P
     164323-41-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (intermediate for prepn. of O-acylglycerol cyclic phosphate as DNA
        polymerase inhibitor)
ΙT
     72741-18-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (phosphorylating agent as intermediate for prepn. of O-acylglycerol
        cyclic phosphate as DNA polymerase inhibitor)
ΙT
     538-37-4, Dibenzyl phosphorochloridate
                                             777-52-6, p-Nitrophenyl
     dichlorophosphate
                         793-10-2, 4-Nitrophenyl phenyl phosphorochloridate
     2524-64-3, Diphenyl phosphorochloridate
                                                             17672-53-6,
                                              16062-77-4
     Bis(2,2,2-trichloroethyl) phosphorochloridate
                                                    17677-92-8,
     Bis(2,2,2-trichloro-1,1-dimethylethyl) phosphorochloridate
                                                                   23561-36-6,
     2-Chloromethyl-p-nitrophenyl dichlorophosphate
                                                       51766-21-3, Phenyl
                          ochloridate 57188-46-2, Bis(p-nitrobenzyl)
59346-65-5, Di-tert-butyl phosphorobromidate
     N-phenylphosphoramidochloridate
     phosphorochloridate
     85363-77-5, Bis[2-(p-nitrophenyl)ethyl] phosphorochloridate
                                                                   164215-58-1,
     2-(N, N-Dimethylamino)-4-nitrophenyl phosphorochloridate
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphorylating agent for prepn. of O-acylglycerol cyclic phosphate as
        DNA polymerase inhibitor)
IT
     151766-47-1P 151766-51-7P 151766-52-8P
     151766-53-9P 164215-56-9P
     RL: SPN (Synthetic preparation); THU (Therapeutic use)
     ; BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of O-acylglycerol cyclic phosphate as DNA polymerase inhibitor
        and antitumor agent)
IT
     334-88-3, Diazo methane
                               14347-83-2, 1-O-Benzyl-2, 3-O-isopropylidene-sn-
                             19670-51-0, (.+-.)-1-O-Hexadecanoylglycerol
               16495-03-7
     glycerol
     21406-61-1, Pentyltriphenylphosphonium bromide
                                                      22323-82-6
                                                                    50889-30-0,
     (6-Carboxyhexyl)triphenylphosphonium bromide 89395-28-8
                                                                115268-48-9,
     (.+-.)-1-0-Hexadecanoyl-2,3-0-isopropylideneglycerol
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction in prepn. of O-acylglycerol cyclic phosphate as DNA
        polymerase inhibitor)
IT
     9012-90-2, DNA polymerase
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (.alpha.; prepn. of O-acylglycerol cyclic phosphate as DNA polymerase
        inhibitors)
     151766-47-1P 151766-51-7P 151766-52-8P
IT
     151766-53-9P 164215-56-9P
     RL: SPN (Synthetic preparation); THU (Therapeutic use)
     ; BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of O-acylglycerol cyclic phosphate as DNA polymerase inhibitor
```

and antitumor agent)

RN 151766-47-1 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Na

RN 151766-51-7 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4S)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Na

RN 151766-52-8 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 151766-53-9 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4S)-2-hydroxy-2-oxido-1,3,2-

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

dioxaphospholan-4-yl]methyl ester, sodium salt, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 164215-56-9 HCAPLUS

CN Hexadecanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

Na

L24 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1995:285626 HCAPLUS

DN 122:75127

TI Phospholipids containing two different unsaturated fatty acids for use in therapy, nutrition, and cosmetics

IN Horrobin, David; McMordie, Austin; Manku, Mehar Singh

PA Scotia Holdings PLC, UK

SO Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM C07F009-10

ICS A61K031-66; A61K007-00; A23J007-00; C07F009-117

CC 6-5 (General Biochemistry)

Section cross-reference(s): 1, 17, 62

FAN.CNT 1

	J. 1. 1			
	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
ΡI	EP 609078	Al 19940803	EP 1994-300599	19940127
		CH, DE, DK, ES, FR,	GB, GR, IE, IT, LI,	LU, MC, NL, PT, SE
	CA 2114349	AA 19940728		19940127
	NO 9400288	A 19940728	NO 1994-288	19940127
	AU 9454749	Al 19940804	AU 1994-54749	19940127
	AU 671329	B2 19960822		
	ZA 9400587	A 19940909	ZA 1994-587	19940127

RL: BUU (Biological use, unclassified); FFD (Food or feed use); SPN

(phospholipids contg. two different unsatd. fatty acids for use in

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

160109-97-7 HCAPLUS

RN

therapy, nutrition, and cosmetics)

6,9,12-Octadecatrienoic acid, 1-[[(2-oxido-1,3,2-dioxaphospholan-2-yl)oxy]methyl]-1,2-ethanediyl ester, (all-2)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

160109-96-6P IT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (phospholipids contg. two different unsatd. fatty acids for use in

therapy, nutrition, and cosmetics) 160109-96-6 HCAPLUS

RN

6,9,12-Octadecatrienoic acid, 3-[(2-oxido-1,3,2-dioxaphospholan-2-yl)oxy]-CN 2-[(1-oxo-9-octadecenyl)oxy]propyl ester, (all-Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

- (CH2)4

```
ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2003 ACS
     1995:255353 HCAPLUS
DN
     122:31708
     Dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as antiinflammatory
IN
     Johnson, Roy A.
PA
     Upjohn Co., USA
so
     U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 717,428, abandoned.
     CODEN: USXXAM
DT
     Patent
LA
     English
     ICM C07C261-00
IC
NCL
     558158000
     29-7 (Organometallic and Organometalloidal Compounds)
     Section cross-reference(s): 1
     PATENT NO.
                        KIND DATE
                                             APPLICATION NO.
                                                                  DATE
PI
     US 5347029
                         Α
                               19940913
                                               US 1993-168441
                                                                  19931216
     CA 2102303
                         AA
                               19921220
                                               CA 1992-2102303
                                                                  19920521
     AT 164163
                               19980415
                         Ε
                                               AT 1992-913025
                                                                  19920521
PRAI US 1991-717428
                               19910619
     MARPAT 122:31708
AB
     Provided are novel dialkyl (dialkoxyphosphinyl)methyl phosphates
     (R1O) 2P(O) CH(CH2NR2R3) OP(O) (OR1) 2 which are useful as antiinflammatory and
     anti-arthritic agents. The compds. are synthesized from the reaction of
     tetra-Et oxiranylidenebisphosphonate and unsubstituted or alkylamines.
     Representative compd. include 2-(benzylamino)-1-
     (diethoxyphosphinyl) ethylphosphonic acid di-Et ester, 1-
     (diethoxyphosphinyl)-2-[2'-(1',2',3',4'-tetrahydro)naphthylamino]ethylphosphonic acid di-Et ester, 2-(3-fluorobenzylamino)-1-
     (diethoxyphosphinyl)ethylphosphonic acid di-Et ester, and
     5,5-dimethyl-2-[2-(3-fluorobenzyl)amino-1-[(5,5-dimethyl-1,3,2-dioxaphosphorinan-2-yl)oxy]ethyl]-1,3,2-dioxaphosphorinane P,2-dioxide.
     dialkoxyphosphinylaminoethyl phosphate; antiinflammatory
     dialkoxyphosphinylaminoethyl phosphate; antiarthritic
     dialkoxyphosphinylaminoethyl phosphate
IT
     Inflammation inhibitors
         (prepn. of dialkyl (dialkoxyphosphinyl)aminoethyl phosphates as
        antiinflammatory and antiarthritic agents)
IT
     Inflammation inhibitors
         (antiarthritics, prepn. of dialkyl (dialkoxyphosphinyl)aminoethyl
        phosphates as antiinflammatory and antiarthritic agents) 1777-74-4P 146777-75-5P 146777-76-6P 146777-77-7P
     146777-74-4P
                                                                       146777-78-8P
     146777-79-9P
                     146777-80-2P
                                      146777-81-3P
                                                      146777-82-4P
                                                                       146777-83-5P
                     146777-85-7P
     146777-84-6P
                                      146777-86-8P 146777-87-9P
     146777-88-0P
                     159759-67-8P
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RL: BAC (Biological activity or effector, xcept adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as
        antiinflammatory and antiarthritic agents)
IT
     61-54-1, Tryptamine
                            64-04-0, Phenethylamine
                                                      91-00-9,
                           100-46-9, Benzylamine, reactions 100-82-3, 107-11-9, Allylamine 108-91-8, Cyclohexylamine,
     Aminodiphenylmethane
     3-Fluorobenzylamine
     reactions
                141-43-5, Ethanolamine, reactions
                                                      501-53-1, Benzyl
     chloroformate
                    1660-94-2
                                  2954-50-9
                                             3731-52-0, 3-(Aminomethyl)pyridine
     3886-69-9, (R)-(+)-1-Phenylethylamine
                                              5036-48-6, 1-(3-
     Aminopropyl)imidazole 30525-89-4, Paraformaldehyde
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as
        antiinflammatory and antiarthritic agents)
IT
                   37465-31-9P 141828-19-5P
     35335-22-9P
                                                146777-89-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as
        antiinflammatory and antiarthritic agents)
IT
     146777-87-9P 146777-88-0P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as
        antiinflammatory and antiarthritic agents)
RN
     146777-87-9 HCAPLUS
CN
     1,3,2-Dioxaphosphorinane-2-ethanamine, .beta.-[(5,5-dimethyl-2-oxido-1,3,2-
     dioxaphosphorinan-2-yl)oxy]-N-[(3-fluorophenyl)methyl]-5,5-dimethyl-,
     2-oxide (9CI) (CA INDEX NAME)
```

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L24 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2003 ACS AN 1986:533669 HCAPLUS
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DN 105:133669

ΤI Aminopurine derivatives

PA Beecham Group PLC, UK

Jpn. Kokai Tokkyo Koho, 14 pp. SO

CODEN: JKXXAF

DT Patent

Japanese LA

ICM C07D473-32 IC ICS C07F009-65

ICA A61K031-52

26-9 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1 FAN.CNT 3

FAN.	CNT	3							
	PA'	TENT NO.		KIND	DATE		API	PLICATION NO	DATE
PI	JP	61085388		A2	19860430		JP	1985-207693	19850919
	JP	05086792		B4	19931214				
	EP	182024		A2	19860528		EP	1985-111354	19850909
	EP	182024		EA.	19890308				
	EΡ	182024		B1	19910403				
		•	CH,	DE, FR	, GB, IT,	LI,	LU, t	NL, SE	
		8504246		A			DK	1985-4246	19850918
	-	167019		B1	19930816			•	
		8547560		Al	19860327		AU	1985-47560	19850918
		589371		BS	19891012				
		8507149		A	19860827			1985-7149	
		1262899		A1	19891114			1985-491028	
		547128		A1	19870301			1985-547128	
		283721		B6	19980617			1991-3915	
		06025241		A2	19940201		J₽	1993-130044	19930507
		08026021		B4	19960313				
PRAI		1984-2383		A	19840920				
		1985-1033		A	19850423				
	GB	1985-2061	.8	A	19850816				
GI									

R1OCH2CHCH2OR2

I

```
AB
     Title compds. I (R1, R2 = H, acyl, phosphate, etc.) and their salts,
     useful as virucides (no data), were prepd. Thus, refluxing 0.54 g
     2-amino-6-chloro-9-chloro-9-[2-(2,2-dimethyl-1,3-dioxan-3-yl)ethyl]purine
     with 450 mg 10% Pd/C in ethanol and cyclohexane gave 36%
     2-amino-9-[4-hydroxy-3-(hydroxymethyl)-but-1-yl]purine.
ST
     aminopurine ethylpropanediol prepn virucide
IT
     Virucides and Virustats
        (aminopurine derivs.)
     97845-59-5P
TT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and redn. of)
IT
     104227-86-3P
                                   104227-88-5P
                                                  104227-89-6P
                    104227-87-4P
                                                                  104227-90-9P
     104227-91-0P
                                                  104227-94-3P
                    104227-92-1P
                                   104227-93-2P
                                                                  104227-95-4P
     104227-96-5P
                    104227-97-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of, as virucide)
IT
     104227-96-5P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of, as virucide)
     104227-96-5 HCAPLUS
RN
CN
     9H-Purin-2-amine, 9-[2-(2-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-5-
     yl)ethyl]- (9CI) (CA INDEX NAME)
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L24
    ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2003 ACS
AN
     1986:514844 HCAPLUS
DN
     105:114844
TI
     Cyclic phosphate esters of substituted 9-(1,3-dihydroxy-2-
     propoxymethyl) purines
IN
     Prisbe, Ernest J.; McGee, Daniel P. C.
PA
     Syntex (U.S.A.), Inc., USA
so
     U.S., 4 pp.
     CODEN: USXXAM
DT
     Patent
     English
LA
IC
     ICM C07D473-18
     ICS A61K031-52
NCL
     544276000
     26-9 (Biomolecules and Their Synthetic Analogs)
CC
     Section cross-reference(s): 1, 29
FAN.CNT 1
     PATENT NO.
                      KIND DATE
                                           APPLICATION NO. DATE
```

PI US 4590269 A 19860520 US 1984-594508 19840329 PRAI US 1984-594508 19840329 OS CASREACT 105:114844 GI

AB The title compds. [I; Y = OH, NH2; Z = H, (un) substituted hydrocarbyl,cation], useful as antiviral agents (no data), were prepd. Thus, 9-(1,3-dihydro-2-propoxymethyl) guanine in MeCN was reacted with SnCl4 and pyrophosphoryl chloride, followed by workup and chromatog, with NH4OH eluent, to give I (Y = OH, Z = NH4). purine cyclic phosphate prepn antiviral Virucides and Virustats ΙT ((dihydroxypropoxymethyl)purine cyclic phosphate esters) 13498-14-1 RL: RCT (Reactant); RACT (Reactant or reagent) (phosphorylation by, of (dihydroxypropoxymethyl) guanine) IT 10025-87-3 RL: RCT (Reactant); RACT (Reactant or reagent) (phosphorylation by, of diamino(dihydroxypropoxymethyl)purine) IΤ 82410-32-0 86629-59-6 RL: RCT (Reactant); RACT (Reactant or reagent) (phosphorylation of) IT 91516-85-7P 91516-89-1P 100683-67-8P 104145-76-8P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of, as antiviral agent) IT 91516-85-7P 91516-89-1P 100683-67-8P 104145-76-8P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[(2-hydroxy-2-oxido-1,3,2-

dioxaphosphorinan-5-yl)oxy]methyl]- (9CI) (CA INDEX NAME)

(Preparation); USES (Uses)

91516-85-7 HCAPLUS

RN

CN

(prepn. of, as antiviral agent)

RN 91516-89-1 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[(2-hydroxy-2-oxido-1,3,2dioxaphosphorinan-5-yl)oxy]methyl]-, monoammonium salt (9CI) (CA INDEX

#### ● инз

RN

100683-67-8 HCAPLUS
9H-Purine-2,6-diamine, 9-[[(2-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-5-yl)oxy]methyl]- (9CI) (CA INDEX NAME) CN

RN 104145-76-8 HCAPLUS

CN 9H-Purine-2, 6-diamine, 9-[[(2-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-5yl)oxy]methyl]-, monoammonium salt (9CI) (CA INDEX NAME)

NH3

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ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2003 ACS
     1986:207063 HCAPLUS
AN
     104:207063
DN
     N-Alkylguanine acyclonucleosides as antiviral agents
TI
IN
     Maccoss, Malcolm; Tolman, Richard L.; Strelitz, Robert A.
     Merck and Co., Inc., USA
Eur. Pat. Appl., 29 pp.
PA
SO
     CODEN: EPXXDW
DT
     Patent
LA
     English
IC
     ICM C07D473-18
     ICS C07F009-65; A61K031-52; A61K031-675
     26-9 (Biomolecules and Their Synthetic Analogs)
     Section cross-reference(s): 1, 63
FAN.CNT 1
     PATENT NO.
                       KIND DATE
                                             APPLICATION NO.
                                                               DATE
                       A1
                             19851121
                                             EP 1985-400613
                                                               19850328
         R: CH, DE, FR, GB, IT, LI, NL
     US 4579849
                             19860401
                                             US 1984-597785
                                                               19840406
                       A
JP 60228480
PRAI US 1984-597785
                        A2
                             19851113
                                             JP 1985-71333
                                                               19850405
                             19840406
     CASREACT 104:207063
GT
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AB The title compds. I [R1,R2 = C1-19 (halo)alkyl, -alkenyl, -alkynyl or R2 =H; R3 = H, C1-6 alkyl, -hydroxyalkyl; R4 = H, halo, C1-4 alkyl, NH2; R5, R6, R7 = H, OH, C1-6 alkyl, C1-8 acyloxy, C1-6 alkoxy, PO3-, or 2 of R5, R6 = R7 = (-OPO2O-)-, etc.; Z = O, S, CR2; X = anion] useful as antiviral agents (no data) were prepd. Thus, to (S)-9-(2,3-dihydroxy-1propoxymethyl) guanine in DMSO was added K2CO3 followed by MeI to give (S)-I (R1, R2 = Me; R3, R4 = H; R5, R6 = OH; R7 = Me; X = I) (II). A water-sol. cintment contained II 0.5, glycerol 15, Macrogol 300 20, and PEG 1500 64.5 g. alkylguanine acyclonucleoside prepn antiviral pharmaceutical; guaninium acyclonucleoside prepn antiviral; antiherpetic acyclonucleoside guaninium; quaternization guanine acyclonucleoside; virucide guanine acyclonucleoside ΙŤ Quaternization (of guanine acyclonucleosides) Virucides and Virustats IT

(N-alkylguanine acyclonucleosides)

IT Nucleosides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(acyclo-, N-alkyl, prepn. of, as antiviral agents)

IT 75-03-6 107-08-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of (dihydroxypropoxymethyl)guanine)

IT 82410-32-0

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Sackey 09/937386 Page 171
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RL: RCT (Reactant); RACT (Reactant or reagent)
        (alkylation of)
     102052-81-3
                  102052-83-5
                                 102052-85-7
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (as antiviral agent)
IT
    111-64-8
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (esterification of, with methyl(dihydroxypropoxymethyl)quanine)
IT
    59277-89-3
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (methylation of)
                   102052-86-8P
IT
    102052-68-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and quaternization of)
IT
    82145-52-6P
                  102052-67-5P
                                  102052-69-7P
    RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of)
    102052-70-0P
IT
                    102052-71-1P
                                   102052-72-2P
                                                  102052~73-3P
                                                                 102052-74-4P
     102052-75-5P
                    102052-76-6P 102052-77-7P 102052-79-9P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of, as antiviral agent)
T T
                  102052-78-8
    96480-03-4
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (quaternization of)
ΙT
    102052-77-7P 102052-79-9P
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of, as antiviral agent)
RN
    102052-77-7 HCAPLUS
    1H-Purinium, 2-amino-6,9-dihydro-9-[[(2-hydroxy-2-oxido-1,3,2-
     dioxaphosphorinan-5-yl)oxy]methyl]-7-methyl-6-oxo-, inner salt (9CI) (CA
    INDEX NAME)
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# \*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*

=> d que

STR

REP G1=(0-3) C
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 8
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RSPEC I NUMBER OF NODES IS

STEREO ATTRIBUTES: NONE

L5 2167 SEA FILE=REGISTRY SSS FUL L3

L16 STR

J.

CH2·C~~O @16 17 18

CH2·O~C~O @12 13 14 15

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Sack y 09/937386 Pag 173
REP G1 = (0-3) C
VAR G2=H/AK/10/12/16
NODE ATTRIBUTES:
CONNECT IS E1 RC AT CONNECT IS E1 RC AT
                        8
                      15
CONNECT IS E1 RC AT 18
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 18
STEREO ATTRIBUTES: NONE
L18
           2139 SEA FILE=REGISTRY SUB=L5 SSS FUL L16
           1246 SEA FILE=HCAPLUS ABB=ON L18
L19
             30 SEA FILE=HCAPLUS ABB=ON L19(L)THU/RL
L20
L21
            715 SEA FILE=HCAPLUS ABB=ON L19(L) (PREP OR SPN OR IMF)/RL
             21 SEA FILE=HCAPLUS ABB=ON L20 AND L21
L24
           1450 SEA FILE=REGISTRY ABB=ON L18 AND 1-2/NR
L26
           1008 SEA FILE=HCAPLUS ABB=ON L26
L27
             18 SEA FILE=HCAPLUS ABB=ON L27(L)THU/RL
L28
L29
               5 SEA FILE=HCAPLUS ABB=ON (L24 OR L28) NOT L24
=> d 129 all 1-5 hitstr
L29 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS
     2002:905886 HCAPLUS
AN
DN
     137:379994
ΤI
     Cancerous metastasis inhibitors containing carbacyclic phosphatidic acid
     derivatives
     Mukai, Mutsuko; Kobayashi, Susumu; Murofushi, Hiromu; Murofushi, Kimiko
IN
PA
     Gencom Corporation, Japan
     PCT Int. Appl., 58 pp.
SO
     CODEN: PIXXD2
DΤ
     Patent
LA
     Japanese
IC
     ICM A61K031-662
     ICS A61P035-04; C07F009-6574
     1-6 (Pharmacology)
     Section cross-reference(s): 28
FAN.CNT 1
     PATENT NO.
                       KIND DATE
                                             APPLICATION NO. DATE
PI
     WO 2002094286
                       Al
                             20021128
                                             WO 2002-JP4839
                                                               20020520
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, S2, TZ, UG, ZM, 2W, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI JP 2001-150685
                             20010521
OS
     MARPAT 137:379994
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GI

Ι

AB The invention aims at providing novel cancerous metastasis inhibitors by examg. carbacyclic phosphatidic acid derivs. for inhibitory activity against the infiltration of cancer cells. The invention provides cancerous metastasis inhibitors contg. as the active ingredient compds. represented by the general formula I (R is linear or branched C1-30 alkyl, linear or branched C2-30 alkenyl, or linear or branched C2-30 alkynyl, with the proviso that each group may contain a cycloalkane ring or an arom. ring; and M is hydrogen or a counter cation).

ST cancerous metastasis inhibitor carbacyclic phosphatidate deriv antimelanoma

IT Melanoma

(B16; cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Animal cell line

(HT-1080, infiltration; cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Human

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Lysophosphatidic acids

RL: BSU (Biological study, unclassified); BIOL (Biological study) (cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Lung, neoplasm

(metastasis, from melanoma; cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Antitumor agents

Neoplasm

(metastasis; cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 60-92-4, CAMP

RL: BSU (Biological study, unclassified); BIOL (Biological study) (cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 476310-13-1P 476310-14-2P 476310-15-3P

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 164215-56-9 172360-60-0 476310-07-3

476310-08-4 476310-09-5 476310-10-8

476310-11-9 476310-12-0

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 2930-05-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(canc rous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 476310-16-4P 476310-17-5P 476310-18-6P 476310-19-7P 476310-20-0P 476310-21-1P 476310-22-2P 476310-23-3P 476310-24-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

(1) Bestmann, H; Chemical Ber 1992, VO.125(1), P225 HCAPLUS

(2) Sagami Chemical Research Center; JP 06-228169 A 1994 HCAPLUS

(3) Sagami Chemical Research Center; JP 09-25235 A 1997 HCAPLUS

(4) Yeda Research And Development Co Ltd; WO 0057864 A 2000 HCAPLUS

(5) Yeda Research And Development Co Ltd; EP 1162979 A 2000 HCAPLUS

(6) Yeda Research And Development Co Ltd; AU 3451600 A 2000

(7) Yokomatsu, T; Heterocycles 1997, V46, P463 HCAPLUS

IT 164215-56-9 172360-60-0 476310-07-3

476310-08-4 476310-09-5 476310-10-8

476310-11-9 476310-12-0

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

RN 164215-56-9 HCAPLUS

CN Hexadecanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

Na

RN 172360-60-0 HCAPLUS

CN 9-Hexadecynoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-y1)methyl
ester, sodium salt (9CI) (CA INDEX NAME)

Na

RN 476310-07-3 HCAPLUS

CN 5,8,11,14,17-Eicosapentaenoic acid, (2-hydroxy-2-oxido-1,3,2-

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

PAGE 1-A

$$CH_2-O-C-(CH_2)_3-CH=CH-CH_2-CH=CH-CH_2-CH=$$

Na

PAGE 1-B

= CH- CH $_2-$  CH= CH- CH $_2-$  CH= CH- Et

RN 476310-08-4 HCAPLUS
CN 4,7,10,13,16,19-Docosahexaenoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

PAGE 1-A

Na

PAGE 1-B

= CH- CH2- CH= CH- CH2- CH= CH- CH2- CH= CH- Et

RN 476310-09-5 HCAPLUS

1,3,2-Dioxaphospholane, 4-[[[8-[(1R,2S)-2-hexylcyclopropyl]octyl]oxy]methy
1]-2-hydroxy-, 2-oxide, sodium salt, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Na

RN 476310-10-8 HCAPLUS

CN 1,3,2-Dioxaphospholane, 4-{(hexadecyloxy)methyl}-2-hydroxy-, 2-oxide, sodium salt (9CI) (CA INDEX NAME)

Na

RN 476310-11-9 HCAPLUS

CN Carbamic acid, [7-[(1R,2S)-2-hexylcyclopropyl]heptyl]-, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, monosodium salt, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Na

RN 476310-12-0 HCAPLUS

CN Carbamic acid, pentadecyl-, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, monosodium salt (9CI) (CA INDEX NAME)

Na

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L29 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2003 ACS
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AN 2001:834204 HCAPLUS

DN 136:145102

TI Neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells

AU Haimovitz, Rachel; Shinitzky, Meir

CS Department of Biological Chemistry, The Weizmann Institute of Science, Rehovot, 76100, Israel

SO Life Sciences (2001), 69(23), 2711-2723

CODEN: LIFSAK; ISSN: 0024-3205

PB Elsevier Science Inc.

DT Journal

LA English

CC 1-11 (Pharmacology)

A series of cyclic glycerophosphates and their deoxy analogs were tested for induction of neuronal outgrowth in PC12 cells. Under chronic presence of a cyclic phosphate PC12 cells developed distinct isles of neuronal networks which covered up to 20% of the culture area, while .alpha. and .beta. glycerophosphates (the neg. control compds.) did not induce any neuronal outgrowth. Distinct isles of neuronal networks were also obsd. upon short term application (i.e. 2 pulses of 3 h each at day 1 and day 4) of the tested cyclic phosphates in contrast to an analogous short term exposure to NGF which was abortive. Anal. of tyrosine phosphorylation indicated a battery of phosphorylated proteins after several minutes of application of the cyclic phosphates, among which was an ERK protein of .apprx.63kD (possibly ERK7). Nerve rescue expts. were carried out with NGF differentiated PC12 cells where NGF was replaced with either 1,2 or 1,3 cyclic propanediolphosphate (1,2 cPP and 1,3 cPP) for 7 days. A distinct dose dependent preservation of neuronal network by these compds. was obsd. In the control cultures NGF deprivation resulted in massive neuronal retraction and cell death. Preliminary expts. indicated that the nerve rescue by the cyclic phosphates involves the increase in the level of CASPase 6. The above findings suggest that cyclic glycerophosphates and their analogs may bear important physiol. and pharmacol, implications which are currently under investigation.

ST neuron differentiation cyclic phosphate nerve regeneration

IT Nerve

(differentiation; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells)

IT Regeneration, animal

(nerve; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells)

IT Neurotrophic factors

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells)

#### Sackey 09/937386 Page 179 C 11 differentiation IT (neuronal; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) IT Phosphorylation, biological (protein tyrosine; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) IT (regeneration; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) IT Phosphoproteins RL: BSU (Biological study, unclassified); BIOL (Biological study) (tyrosine-contg., phosphorylation; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) IT 182372-15-2, CASPase 6 222838-93-9, Protein kinase ERK7 RL: BSU (Biological study, unclassified); BIOL (Biological study) (neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells IT 57-03-4, .alpha.-Glycerophosphate 60-92-4, CAMP 362-74-3, Dibutyryl CAMP 711-07-9 13507-10-3 17181-54-3, .beta.-Glycerophosphate 20636-79-7 25664-08-8 42320-97-8 286020-33-5 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Abe, N; Molecular Cell Biololgy 1999, V19, P1301 (2) Berridge, M; Annual Review of Biochemistry 1987, V56, P159 HCAPLUS (3) Boulton, T; Cell 1991, V65, P663 HCAPLUS (4) Bredesen, D; Annals of Neurology 1995, V38, P839 MEDLINE (5) Cowley, S; Cell 1994, V77, P841 HCAPLUS (6) Dawson, R; Biochemical Journal 1971, V122, P605 HCAPLUS (7) Frodin, M; Journal of Biological Chemistry 1994, V269, P6207 HCAPLUS (8) Ginty, D; Cell 1994, V77, P713 (9) Glowacka, D; Journal of Neuroscience Research 1990, V25, P453 HCAPLUS (10) Greene, L; Advances in Cellular Neurobiology 1982, V3, P373 HCAPLUS (11) Greene, L; Journal of Cell Biology 1978, V78, P747 HCAPLUS (12) Greene, L; Proceedings of the National Academy of Sciences USA 1976, V73, P2424 HCAPLUS (13) Gunning, P; Journal of Cell Biology 1981, V89, P240 HCAPLUS (14) Gunning, P; Journal of Neuroscience 1981, V1, P1085 HCAPLUS (15) Heidemann, S; Journal of Cell Biology 1985, V100, P916 HCAPLUS (16) Huang, C; Journal of Neurochemistry 1996, V67, P530 HCAPLUS

- (17) Kaplan, D; Nature 1991, V350, P158 HCAPLUS (18) Martin, D; Journal of Neurobiology 1992, V23, P1205 HCAPLUS
- (19) Ohimichi, M; Journal of Biological Chemistry 1992, V267, P21601 (20) Ohimichi, M; Journal of Biological Chemistry 1994, V269, P1143
- (21) Richter-Landsberg, C; Journal Cell Biology 1986, V102, P821 HCAPLUS
- (22) Ross, T; Journal of Biological Chemistry 1986, V261, P11119 HCAPLUS (23) Rouser, G; Biological Membranes 1968, P5 HCAPLUS
- (24) Rydel, R; Proceedings of the National Academy of Sciences USA 1998, V85, P1257
- (25) Shinitzky, M; European Journal of Biochemistry 2000, V267, P2547 HCAPLUS
- (26) Shinitzky, M; Journal of Biological Chemistry 1993, V268, P14109 HCAPLUS
- (27) Young, S; FEBS Letters 1994, V338, P212 HCAPLUS (28) Yung, Y; FEBS Letters 1997, V408, P292 HCAPLUS
- 711-07-9 13507-10-3 20636-79-7 25664-08-8 42320-97-8 286020-33-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells)

RN 711-07-9 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 13507-10-3 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 20636-79-7 HCAPLUS

CN 1,3,2-Dioxaphospholane, 2-hydroxy-4-methyl-, 2-oxide (9CI) (CA INDEX NAME)

RN 25664-08-8 HCAPLUS

CN 1,3,2-Dioxaphospholane-4-methanol, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 42320-97-8 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 286020-33-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

L29 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS

1999:402490 HCAPLUS AN

DN 131:208765

Inhibition of tumor invasion and metastasis by a novel lysophosphatidic TI acid (cyclic LPA)

ΑU Mukai, Mutsuko; Imamura, Fumio; Ayaki, Masako; Shinkai, Kiyoko; Iwasaki, Teruo; Murakami-Murofushi, Kimiko; Murofushi, Hiromu; Kobayashi, Susumu; Yamamoto, Takashi; Nakamura, Hiroyuki; Akedo, Hitoshi

Department of Tumor Biochemistry, Osaka Medical Center for Cancer and CS Cardiovascular Diseases, Osaka, Japan

International Journal of Cancer (1999), 81(6), 918-922 SO CODEN: IJCNAW; ISSN: 0020-7136

PΒ Wiley-Liss, Inc.

DT Journal

English LA

CC 1-6 (Pharmacology)

AB Fetal calf serum (FCS) and 1-oleoyl lysophosphatidic acid (LPA) were previously found to be potent inducers of invasion (transcellular migration) in an in vitro system. A novel LPA, composed of cyclic phosphate and cyclopropane-contg. hexadecanoic acid (PHYLPA), first isolated from myxoamoebae of Physarum polycephalum, and its synthetic derivs. (cLPA) were tested for their ability to inhibit tumor cell invasion and metastasis. Among these, Pal-cLPA, which has a palmitoyl moiety, was most potent in inhibiting invasion, with 93.8% inhibition at the concn. of 25 .mu.M. Invasion in vitro by mouse melanoma cells (B16), human pancreatic adenocarcinoma cells (PSN-1), human lung cancer cells (OC-10) and human fibrosarcoma cells (HT-1080) was also inhibited by Pal-cLPA. The stimulation of MMI cells with LPA triggered F-actin formation, which was impaired by the addn. of Pal-cLPA at invasion-inhibitory concn. Pal-cLPA induced a rapid increase in adenosine 3',5'-cyclic monophosphate (cAMP) concn. in MMI cells. The addn. of dibutyryl cAMP significantly abrogated LPA-induced invasion by MMI cells and actin polymn. in the cells. The inhibition of MM I cell invasion by Pal-cLPA may be ascribed to an increased level of cAMP. Pal-cLPA also suppressed invasion in vitro by MMI cells induced by FCS dose dependently, without affecting proliferation. It also suppressed the pulmonary metastasis of B 16 mouse melanoma cells injected into the tail vein of C57BL/6 mice. Thus, Pal-cLPA is effective in inhibiting invasion and

168217-10-5 169736-88-3 188171-56-4 188171-62-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of tumor invasion and metastasis by a novel lysophosphatidic acid derivs.)

RN 151766-47-1 HCAPLUS

Cyclopropaneoctanoic acid, 2-hexyl-, {(4R)-2-hydroxy-2-oxido-1,3,2-CN dioxaphospholan-4-yl]methyl ester, sodium salt, (15,2R)- (9CI) (CA INDEX

Absolute stereochemistry. Rotation (+).

Na 🗎

RN 168217-08-1 HCAPLUS

CN Hexadecanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 168217-09-2 HCAPLUS

CN 9-Hexadecenoic acid, {(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (92)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

Na

RN 168217-10-5 HCAPLUS

CN 9-Hexadecynoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• Na

RN 169736-88-3 HCAPLUS

CN 9-Octadecenoic acid (92)-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

Na

RN 188171-56-4 HCAPLUS

CN 9-Hexadecenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (9E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

Na

RN 188171-62-2 HCAPLUS

CN Eicosanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

MARPAT 123:350234

os

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ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS
     1995:951163 HCAPLUS
AN
DN
     123:350234
TI
     Promoters of protein phosphokinase C activation containing
     1-O-acylglycerol 2,3-cyclic phosphate
    Kobayashi, Susumu; Imai, Nobuyuki; Onimura, Kenjiro; Nakamura, Shuko; Murofushi, Kimiko
IN
PA
     Sagami Chem Res, Japan
SO
     Jpn. Kokai Tokkyo Koho, 6 pp.
     CODEN: JKXXAF
DT
     Patent
     Japanese
LA
     ICM C07F009-10
IC
     ICS C07F009-6571; C12N009-00
CC
     63-5 (Pharmaceuticals)
FAN. CNT 1
     PATENT NO.
                      KIND DATE
                                            APPLICATION NO.
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                                            -----
     JP 07149772
                       A2
                            19950613
                                            JP 1993-319186
                                                             19931126
PRAI JP 1993-319186
                            19931126
```

AB A promoter for activation of protein phosphokinase C (PKC) contains 1-O-acylglycerol 2,3-cyclic phosphate [I; R = linear or branched C1-30 alkyl or C2-30 alkenyl optionally contg. a cycloalkane or an arom. ring; M = H, alkali or alk. earth metal, (un)substituted NH4] as the active ingredient. It is useful for the treatment of hypertension, hyperglycemia, and dementia. For example, 1-O-[(9S,10R)-9,10-methanohexadecanoyl]-sn-glycerol 2,3-cyclic phosphate sodium salt (II) in vitro promoted 8.1 times the activity of cPKC.alpha. in an assay using [32P]ATP and leupeptin as compared to the control.

ST acylglycerol cyclic phosphate; promoter protein kinase C activation; hypertension treatment acylglycerol cyclic phosphate; hyperglycemia treatment acylglycerol cyclic phosphate; dementia treatment acylglycerol

cyclic phosphate

IT Antidiabetics and Hypoglycemics

Antihypert nsives

(promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

IT Mental disorder

(dementia, promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

IT 151766-47-1 151766-51-7 151766-52-8

151766-53-9 170908-55-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

IT 141436-78-4, Protein kinase c

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

IT 151766-47-1 151766-51-7 151766-52-8

151766-53-9 170908-55-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

RN 151766-47-1 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Na

RN 151766-51-7 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4S)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Na

151766-52-8 HCAPLUS RN

Cyclopropaneoctanoic acid, 2-hexyl-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1R,2S)- (9CI) (CA INDEX CN NAME)

Absolute stereochemistry.

Na

151766-53-9 HCAPLUS RN

Cyclopropaneoctanoic acid, 2-hexyl-, [(4S)-2-hydroxy-2-oxido-1,3,2-CN dioxaphospholan-4-yl]methyl ester, sodium salt, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

170908-55-1 HCAPLUS RN

Heptadecanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl CN ester, sodium salt, (R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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HO R (CH<sub>2</sub>) 15 Me
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Na

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ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS
L29
     1973:52525 HCAPLUS
AN
DN
     78:52525
     Novel phosphate anthelmintics. 1. Alkyl 2,2-dichlorovinyl methyl
TI
     phosphates and related alkoxyalkyl and cycloalkyl analogs of dichlorvos
     Morales, Juan G.; Whetstone, Richard H.; Stoutamire, Donald W.; Hass, D.
υA
     Kendall
     Biol. Sci. Res. Cent., Shell Dev. Co., Modesto, CA, USA
CS
     Journal of Medicinal Chemistry (1972), 15(12), 1225-31
SO
     CODEN: JMCMAR; ISSN: 0022-2623
DT
     Journal
     English
LA
     1-3 (Pharmacodynamics)
CC
     Section cross-reference(s): 23
     Alkyl 2,2-dichlorovinyl Me phosphates showed anthelmintic activity which
AB
     increased with increasing chain length (hydrophobicity) to a max. at
     C7-C10. Thus, 2,2-dichlorovinyl n-heptyl Me phosphate (I) [23248-43-3]
     showed an ED50 of 2 mg/kg orally against Syphacia obvelata in mice, with a
     max. tolerated dose of 500 mg/kg, and gave 50% inhibition of fly head
     cholinesterase [9001-08-5] at 2.5 .tim. 10-10M. N-decyl 2,2-dichlorovinyl
     Me phosphate [23248-45-5] gave max. inhibition of Hymenolepis nana in mice
     (ED50 16 mg/kg orally, max. tolerated dose 500 mg/kg). The C2-C4
     .omega.-chloroalkyl esters and the di-Pr and di-Bu esters had higher
     therapeutic indexes than the asymmetric n-alkyl analogs. To synthesize I,
     dichlorvos was refluxed with KI in Me2CO to form Na 2,2-dichlorovinyl Me
     phosphate, which was converted to the acid with HCl. This acid was
     converted with SOC12 to P,P'-bis(2,2-dichlorovinyl) P,P'-dimethyl
     pyrophosphate, which underwent alcoholysis with n-heptanol to form I.
     dichlorvos analog anthelmintic; phosphate alkyl chlorovinyl anthelmintic
ST
     Molecular structure-biological activity relationship
IT
        (anthelmintic, of dichlorvos analogs)
IT
     Anthelmintics
        (dichlorvos analogs)
                                                           3309-70-4
              71-98-7 72-00-4
                                  2597-51-5 3212-19-9
IT
     62-73-7
                 5301-38-2 5301-43-9 5301-54-2 13445-62-0 17196-86-0
     5266-08-0
                               17196-89-3
                                                         18795-58-9
                                           17196-92-8
                  17196-88-2
     17196-87-1
                                            23248-41-1
                                                         23248-42-2
                  20202-93-1
                               23248-40-0
     20202-81-7
                                                         25561-01-7
                               23248-45-5
                                            23248-46-6
     23248-43-3
                  23248-44-4
                                            34622-78-1
                                                         34641-40-2
                               34622-70-3
     34622-68-9
                  34622-69-0
                               40282-68-6
                                            40282-70-0
                                                         40282-76-6
                  40282-65-3
     35075-19-5
                                                         40282-90-4
                  40282-81-3
                               40282-82-4
                                            40282-88-0
     40282-78-8
                                            40282-98-2
                                                         40282-99-3
                               40282-97-1
     40282-95-9
                  40282-96-0
                               40283-03-2 40283-04-3 40284-62-6
     40283-00-9
                  40283-02-1
     40929-79-1
     RL: BAC (Biological activity or effector, except adv rse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
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